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FACING THE NEGATIVE IMPACT OF CANCER TREATMENT ON FERTILITY

Fertility-related communication and reproductive concerns following a cancer diagnosis

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To my family

ABSTRACT

Background Having children is an important part of life for many men and women. However, cancer treatment may have a negative impact on fertility by, for example, affecting eggs or sperm production. In order to safeguard patients' future ability to have biological children, fertility preservation may be available, such as cryopreservation of sperm or embryo. Even though earlier research show that men and women are positive towards discussing future fertility at the time of diagnosis, many report deficiencies in fertility-related communication and express regret over not having been offered fertility preservation.

Aim The overall aim of this thesis was to study the perceptions and experiences of fertility-related communication among men and women of reproductive age diagnosed with cancer in Sweden. An additional aim was to investigate the experiences of receiving treatment with a potential negative impact on fertility and how this is experienced over time.

Methods The thesis is based on two studies: a quantitative survey study among cancer survivors three to seven years after a cancer diagnosis and a qualitative longitudinal interview study among newly diagnosed cancer patients. In Study 1, 484 cancer survivors (328 women and 156 men; 60% response rate) responded to a study-specific questionnaire including standardized instruments for measuring mental health (SF-36) and infertility-related stress (FPI). In Study 2, newly diagnosed cancer patients participated in individual semi-structured interviews at two time-points, a short time after cancer diagnosis (11 women and 10 men) and two years later (9 women and 7 men).

Results Study 1 showed marked sex differences in recalled fertility-related communication: while the majority of the men had discussed the risk of infertility (80%) and fertility preservation (68%), few women did so (48% and 14%, respectively). In addition, more than half of the men used fertility preservation (54%), while only 2% of the women did so. The majority of the survivors who had a pre-treatment desire to have children still wanted children three to seven years later. In addition, 17% of those who had no pre-treatment desire for children had changed their mind about wanting children after treatment. Study 2 showed that women generally had negative experiences of communicating fertility-related issues, while men felt that they had received extensive information and had been encouraged to bank sperm. Men and women described how the risk of infertility had impacted their experiences over the two years, from being of little concern to affecting decisions concerning future childbearing, causing relationship problems and creating feelings of losing control.

Conclusion The risk of infertility after cancer may cause reproductive concerns among both men and women, and according to the results women are particularly vulnerable. In view of the complexity of fertility preservation for female cancer patients, clear guidelines and close collaboration between cancer clinics and reproduction clinics may help in the effort to improve fertility-related communication with women of reproductive age.

LIST OF PUBLICATIONS

This doctoral thesis is based on the following studies, referred to in the text by their Roman numerals:

I. Armuand, G. M., Rodriguez-Wallberg, K. A., Wettergren, L., Ahlgren, J., Enblad, G., Höglund, M., & Lampic, C. (2012). Sex Differences in Fertility-Related Information Received by Young Adult Cancer Survivors. Journal of Clinical Oncology, 30(17), 2147-2153.

II. Armuand, G. M., Wettergren, L., Rodriguez-Wallberg, K. A., & Lampic, C. (2014). Desire for children, difficulties achieving a pregnancy, and infertility distress 3 to 7 years after cancer diagnosis. Supportive Care in Cancer, 22(10), 2805-2812.

III. Armuand, G. M., Wettergren, L., Rodriguez-Wallberg, K. A., & Lampic, C. (2015). Women more vulnerable than men when facing risk for treatment-induced infertility: A qualitative study of young adults newly diagnosed with cancer. Acta Oncologica, 54(2), 243-252.

IV. Armuand, G. M., Wettergren, L., Nilsson, J., Rodriguez-Wallberg, K. A., & Lampic, C. Finding my way: A longitudinal study exploring cancer patients' experiences of threatened fertility. Submitted.

CONTENTS

LIST OF ABBREVIATIONS

ART	Assisted Reproductive Technologies
FP	Fertility Preservation
FPI	Fertility Problem Inventory
IVF	In Vitro Fertilization
QoL	Quality of Life
SB	Sperm Banking
SF-36	Short-Form 36 Health Survey

KEY CONCEPTS

Patient The origin of "patient" comes from the Latin p*atiēns*, meaning to endure. Defined as 1) being able to tolerate delays or to show understanding, or being capable of endure problems, pain or suffering without becoming annoyed or anxious and 2) a person receiving medical attention, care or treatment (American Heritage Dictionary, 2011). A concept analysis by Kasén (2012) defines a patient as a person who undergoes or receives care. Based on the values in caring science, it is essential that the patient is allowed to be a suffering human being; the patient must be recognized as a person in a vulnerable state, where his or her dignity are at risk of violation, and is therefore in need of protection and care. In this thesis, the wording is also used to indicate a person who at the time of study undergoes initial cancer treatment.

Cancer survivor The term "cancer survivor" was introduced by the National Coalition for Cancer Survivorship (NCCS) as a motivating psychosocial term in order to 'empower patients to make decisions about their care and to push for better research and treatment' (Clark & Stovall, 1996). When the term came to use in research, the definition became unclear, going from being defined as individuals who have been disease free for at least five years to including individuals from the moment of diagnosis (Twombly, 2004). In this thesis, the wording is used to indicate individuals who have completed their initial cancer treatment (not including adjuvant anti-oestrogen therapy and chemotherapy treatment by oral administration). However, it is important to remember that not all persons who have been treated for cancer want to be defined as cancer survivors as the label does not describe their identity, or implies a role they do not want to take on (Khan, Harrison, Rose, Ward, & Evans, 2012).

Communication The origin of "communication" is from the Latin *commūnicātus*, meaning to impart, make common, to share. Defined as 1) imparting or interchange of information, news or ideas. Being able to share and understand each other's thoughts and feelings, 2) pass on or transmit an infectious disease, heat or motion to another, 3) a connecting between two rooms and 4) receive Holy Communion (Oxford dictionaries, 2015). A concept analysis of the Swedish word *kommunikation* by Fredriksson (Fredriksson, 2012) shows how the definition has changed from the meaning *gemenskap* (community, fellowship, solidarity) to "transfer and exchange information". However, in the newer meaning, some nuances of communication are lost, such as finding mutuality or a connection through the communication. Communication in caring unites and enables understanding, but it may also be a source of conflict as it holds an aspect of power: patients in a vulnerable state may more or less lose their ability to communicate their needs. In this thesis, communication is used in order to depict how information about fertility and fertility preservation not only concerns the transmission of fact, but also the dialogue between patients and health care professionals about the patients' needs regarding reproductive issues.

PREFACE

In 2002, I graduated as a registered nurse and worked for several years in haematological and oncological cancer care. However, the motivation for starting my education to become a nurse was that I wanted to do research, and during some courses in reproductive medicine, I had the fortune to be recruited to the research project that came to be this thesis. This was a great opportunity to explore my interests: research methodology, cancer care and reproductive care. Looking back at my work as a nurse, something that strikes me is that we never or rarely discussed the impact of cancer treatments on the patient's future ability to have children. Sure, men were sent to cryopreserve sperm, but we never asked them how they experienced this or how they perceived the risk of future infertility. Women's fertility was never mentioned; it was a non-issue never discussed in the staff group. It is my hope that the research findings can contribute to the further understanding of the psychosocial aspects of oncology care concerning fertility after cancer. In addition to this, I also hope that this thesis will provide health care professionals with the courage to talk about the risk of infertility and about fertility preservation with men and women diagnosed with cancer.

1 BACKGROUND

1.1 CANCER AND THE DESIRE TO HAVE CHILDREN

Books, magazines and the internet are filled with glossy pictures of families and enticing descriptions of parenthood, and most men and women have plans for building a family. The desire to have children is so deeply rooted in our being that starting a family has been recognized as a fundamental human right (Article 16 in the United Nations Universal Declaration of Human Rights). However, the path to achieving desired parenthood is not always easy, and the worldwide prevalence of infertility is at approximately 15% and increasing (Petraglia, Serour, & Chapron, 2013). There are numerous explanations to the increase, and besides nutritional and epidemic infections, three other reasons have been suggested: 1) Delayed childbearing in high income countries with following lower reproductive ability; this especially true among women, where higher age comes with a higher risk for uterine fibroids, endometriosis, polycystic ovary syndrome and chronic anovulation. Among both men and women, delayed childbearing also comes with a higher risk for being exposed to sexually transmitted diseases, leading to the risk of reduced reproductive ability, with a higher risk of infertility among women. In low income countries the risk is also high among men due to untreated infections. 2) Exposure to biological and psychological stress and environmental pollutants may decrease fertility. 3) Oncologic treatments with a gonadotoxic effect allow patients to survive cancer, but at the cost of their fertility (Petraglia et al., 2013). The latter is where the need for this thesis originated.

In the Nordic countries—Denmark, Finland, Island, Norway and Sweden—approximately 145,000 persons are diagnosed with cancer each year, and almost 10,000 of these are younger than 44 when diagnosed (Engholm et al., 2014). The overall five year survival rate after a cancer diagnosis has been increasing over the last decades, and was approximately 80% (age 0-49) between 2009 and 2012. Today, there are about 78,000 men and women living in the Nordic countries who were younger than 44 at cancer diagnosis (Engholm et al., 2014). When leaving the cancer experience behind, many of these men and women return to everyday life, and studies among cancer survivors show that having biological children is seen a way to achieve normality (Crawshaw & Sloper, 2010; Zebrack, Casillas, Nohr, Adams, & Zeltzer, 2004). A study among female survivors showed that the cancer experience did had no impact on the desire to have children in the majority of the women (68%), while in 15% the desire had increased and in 17% the desire had decreased (Canada & Schover, 2012). A study among male cancer survivors showed that the majority of the men felt that the cancer experience had increased the value they placed on family closeness and felt that the cancer experience had made them, or would make them, better parents (Schover, Brey, Lichtin, Lipshultz, & Jeha, 2002). However, as mentioned above oncological treatment may reduce the possibility of cancer patients having children in the future.

1.2 THE IMPACT OF CANCER ON FERTILITY

Modern cancer treatment includes systemic therapies, where substances are introduced orally or directly to the bloodstream to treat cancer cells anywhere in the body (e.g. chemotherapy or hormone therapy), and local therapies, where the goals is to treat a tumour at the site (i.e. radiation therapy and surgery). Several of these treatments may affect the male and female reproductive ability by affecting, for example, the production of sperm or by damaging the eggs (oocytes) or the uterus (Rodriguez-Wallberg, 2012). Three cohort studies conducted in two Nordic countries have investigated birth rates among cancer survivors. A Norwegian study (Stensheim, Cvancarova, Møller, & Fossa, 2011) compared the post-cancer birth rate among cancer survivors (n=27,556) who had been diagnosed with cancer at age of 16–45 between 1967 and 2004 with the birth rate among a matched control group (n=137,700) from the general population. Observation time was until pregnancy, death, age 46 or December 2006. Cancer survivors presented lower birth rates than controls, with lower rates among women compared to men (hazard ratio [HR] = 0.61 vs. 0.74). Breast cancer and cervical cancer among women and acute leukaemia among both men and women presented the lowest post-cancer birth rates (Stensheim et al., 2011). Another study carried out in Norway (Syse, Kravdal, & Tretli, 2007) included first births among 1.38 million men and 1.24 million women aged 17–44 who were born between 1935 and 1984. Observation time was until conception, death, age 44, emigration or December 2001. Out of these, 3,321 children were born among 13,452 cancer survivors. Compared with the general population, first-birth rates among male survivors were reduced with 24% (odds ratio [OR] = 0.76) and with 27% among female survivors (OR = 0.73). Among women, cancer diagnoses presenting reduced first born rates with OR <0.50 were leukaemia and colon and ovarian cancer. Among men, corresponding diagnoses were colon and eye cancer (Syse et al., 2007). A Finnish study (Madanat et al., 2008) compared the first born rate among 25,784 cancer survivors who had been diagnosed with cancer from ages 0–34 between 1953 and 2004 with the first born rate among siblings (n=4,611). Only first born children delivered more than nine month after diagnosis were included. Compared to siblings, both female survivors (relative risk [RR] = 0.46) and male survivors (RR = 0.57) were less likely to parent a first child. Leukaemia and ovarian and breast cancer presented the lowest probability of parenthood among female survivors, and leukaemia and Hodgkin's lymphoma presented the lowest probability among men (Madanat et al., 2008). In summary, parenthood after cancer was reduced with 24–43% among male cancer survivors and with 27–54% among female survivors. Diagnoses related to high risk of infertility among women were leukaemia, breast cancer and ovarian cancer and leukaemia and Hodgkin's lymphoma among men (Madanat et al., 2008; Stensheim et al., 2011; Syse et al., 2007).

The development of assisted reproductive technologies (ART) and cryopreservation methods has generated new treatment opportunities for men and women facing fertility problems, and it has been argued that the first successful human in vitro fertilization (IVF) in 1978 created a new era: "after IVF" (Franklin, 2012). The new reproductive methods not only enabled conception outside the body, but they also opened new opportunities such as intracytoplasmic

sperm injection, where a single sperm is injected into the oocyte and the freezing of sperm, eggs and embryos for IVF treatments later on. These methods are currently applied to offer fertility preservation (FP) options in many clinical situations, including in connection with cancer treatment after careful assessment of clinical indications (Rodriguez-Wallberg, Borgström, & Hovatta, 2014).

However, in order to understand the impact of cancer and cancer treatment on fertility, it is important to understand the reproductive structures that may be affected by cancer treatment, as well as what options men and women have in order to reduce the risk of treatment-induced infertility.

1.2.1 Female fertility and cancer

1.2.1.1 The female reproductive system

The female reproductive system carries out several functions: production of female sex hormones to maintain the reproductive cycle; maturation of oocytes; allowance of spermatozoa to travel inside the system to fertilize the oocyte; transportation of embryo; implantation of embryo into uterus and the following pregnancy; and if no fertilization/implantation occurs, menstruation, where the endometrial lining is shed. The female reproductive system consists of the following structures: vulva, vagina, cervix, uterus, fallopian tubes and ovaries (Figure 1).

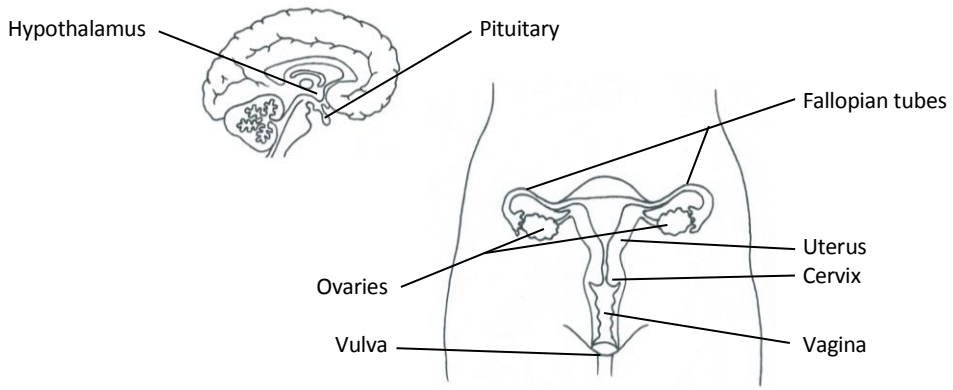

Figure 1. Illustration of the female reproductive system

A narrow passage through the cervix allows sperm to enter the uterus and the fallopian tubes and reach the oocyte that has been captured by the distal part of the tube. After fertilization, the fallopian tubes allow the transportation of the embryo to the uterus cavity. The *uterus* is a

pear-shaped, hollowed structure about 7.5 cm long and 4.5 cm in width, which during pregnancy grows up to 30 cm in length. The *ovaries* are located on both side of the uterus and contain the oocytes and produces hormones. The number of oocytes in the *ovaries* is constantly reducing through life, from approximately 590,000 oocytes at birth to about 360,000 at time of puberty. The remaining number of oocytes in the ovaries is called the ovarian reserve, and about 450 of the oocytes will be ovulated during the woman's reproductive lifetime (Wallace & Kelsey, 2010). When the ovarian reserve is diminished and approximately 1,000 oocytes are left, the women enters menopause, which in Sweden occurs approximately at the age of 50 to 51 (Rödström et al., 2003). The ovaries are under regulation of the hypothalamic–pituitary–gonadal axis through a complex feedback loop where gonadotropin-releasing hormone (GnRH) from the hypothalamus, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary gland (Figure 1) and oestrogen from the ovaries control the menstrual cycle.

1.2.1.2 How do cancer and its treatment affect female fertility?

Chemotherapy, and especially alkylating agents, may reduce the number of oocytes as the toxic effect of the substances may induce apoptosis—programmed cell death—in the oocytes (Rodriguez-Wallberg, 2012; Sabanegh & Ragheb, 2009). Radiation therapy also has a toxic impact as it breaks the DNA in the oocytes. The toxic effects in the ovaries may lead to ovarian failure during or shortly after treatment. But even if a woman maintains her menstrual cycle during the cancer treatment, or regain it shortly afterwards, there is a risk of infertility and premature menopause (before the age of 40) as the ovarian reserve may have been compromised. This leads to a shorter time period for having the desired number of children (Rodriguez-Wallberg, 2012). Among women treated for breast cancer, the majority also undergo adjuvant hormonal treatment with tamoxifen, typically for five years (EBCTCG, 2005; Harlan, Clegg, Abrams, Stevens, & Ballard-Barbash, 2006), which narrows the time-span for childbearing considerably.

Surgery involving the reproductive organs (e.g. ovaries or cervix) can, if not causing permanent infertility (e.g. in connection with hysterectomy), cause sub-fertility, such as obstructions in the fallopian tubes and problems with carrying a pregnancy related to reduced function in the cervix or uterus (Rodriguez-Wallberg, 2012). In young females, radiation therapy directed towards the uterus or the pelvic area may cause scar tissue, reduce the uterine blood circulation and restrict the uterine capacity. This may lead to implantation problems, miscarriage or premature labour. In addition, surgery or radiation therapy towards the brain, such as in connection with brain tumours or total body irradiation, may affect the gonadal axis, with following disruption of the menstrual cycle.

1.2.1.3 Which fertility preservation options are available for women?

Embryo cryopreservation was the first possible, and the most recognized, FP option for women, but recently *cryopreservation of oocytes* has been accepted as an established method (Loren et al., 2013). Retrieval of oocytes is usually performed after hormonal stimulation, or

if there is a contraindication for that treatment in very specific cases, it could be performed during the natural menstrual cycle (Ata, Chian, & Tan, 2010). A stimulated IVF cycle is more effective, as multiple oocytes can be retrieved within a treatment, but it requires time, usually two to six weeks (Rodriguez-Wallberg, 2012). Among women diagnosed with oestrogen-sensitive tumours, the high levels of oestrogen arising during conventional treatment can be harmful, and special stimulating protocols have to be used (Rodriguez-Wallberg & Oktay, 2012b). As cryopreservation of oocytes is now almost as effective as embryo cryopreservation, the choice depends on the woman's preferences. Oocyte cryopreservation may be preferred when very young or when not already in a stable relationship.

In the last decade, research on *cryopreservation of ovarian tissue* has taken a leap, but the technique is still considered experimental, and only around 30 live births have been reported after the procedure (Donnez et al., 2013; Loren et al., 2013). The great advantage with cryopreservation of ovarian tissue is that no waiting period involving hormonal stimulation is needed, and the technique is therefore suitable when cancer treatment cannot wait. A whole ovary or a biopsy of ovarian tissue is collected laparoscopically, dissected into small pieces and cryopreserved (Donnez et al., 2013). To regain fertility after the cancer treatment, the tissue has to be thawed and re-implanted on the ovary or, if both ovaries are absent, in a peritoneal pocket. When the tissue activates, normal hormonal function is restored, and if the woman wants to have children and no natural conception occurs, an ordinary IVF procedure can be performed (Bailey & Ginsburg, 2012). However, caution is advised regarding re-implantation of ovarian tissue in women with disseminated or haematological diseases as there is a risk of retransmission of malignant cells (Lavery, Tsiligiannis, & Carby, 2014).

In connection with cancer in the reproductive organs, conservative fertility-sparing surgery can be used without compromising the wanted effect on the tumour. Examples are *unilateral oophorectomy* in women in connection with the early stages of ovarian cancer, where only the diseased ovary is removed, or *radical trachelectomy* in early stage cervical cancer, where the uterus is spared to enable future pregnancy (Bailey & Ginsburg, 2012). When radiation therapy over the pelvic area is planned, temporarily relocation of the ovaries to outside the radiation area, so-called *oophoropexy* or *ovarian transposition*, can be performed to reduce the risk of radiation damage to the ovaries (Bailey & Ginsburg, 2012). *Radiation shielding* can be used, but requires expertise when planning the radiation field. *Ovarian suppression* with GnRH agonists has been empirically used to protect the ovarian reserve. Research has shown that the toxic effect of chemotherapy on the ovaries is lower among prepubertal girls compared to women of reproductive age. By supressing the gonadal axis, a temporary "prepubertal" state is induced in adult women, with the hope that it will protect the ovarian reserve. However, there is insufficient evidence about the effectiveness of this treatment (Bedoschi, Turan, & Oktay, 2013; Loren et al., 2013).

1.2.1.4 Fertility testing

There is no fertility test that can provide complete knowledge about a woman's fertile ability. If the woman retains her menstrual cycle during cancer treatment, or regains it shortly

afterwards, only trying to get pregnant can give the answer as to whether the women is fertile after completed cancer treatment. If the woman does not want to have children until later, and if there is a risk of premature menopause, the woman can have hormone tests done to measure her ovarian reserve. The test is based on a blood test measuring the glycoproteins secreted from ovarian follicles (cells in the ovary that contain immature oocytes) that are capable of growing. Currently, the most commonly used is the determination of anti-Müllerian hormone (AMH). If high concentrations of this hormone are present in a blood sample, this indicates that a high number of ovarian follicles with potential to grow is present and that fertility may be possible (Rodriguez-Wallberg & Oktay, 2012a). If the AMH levels are low, this may indicate that the ovarian reserve is reduced, with a following risk of premature menopause. In this case, the woman may have to consider whether she has to reprioritize childbearing and have children earlier than she had planned.

1.2.2 Male fertility and cancer

1.2.2.1 The male reproductive system

The male reproductive system has the following functions: production of male sex hormones maintaining the male reproductive system; to produce, maintain, and transport sperm and protective fluid (semen); and to transport sperm into the female reproductive system during intercourse. The male reproductive system mainly consists of the following structures: penis, scrotum, testicles, epididymis, vas deference, urethra, seminal vesicles and the prostate gland (Figure 2).

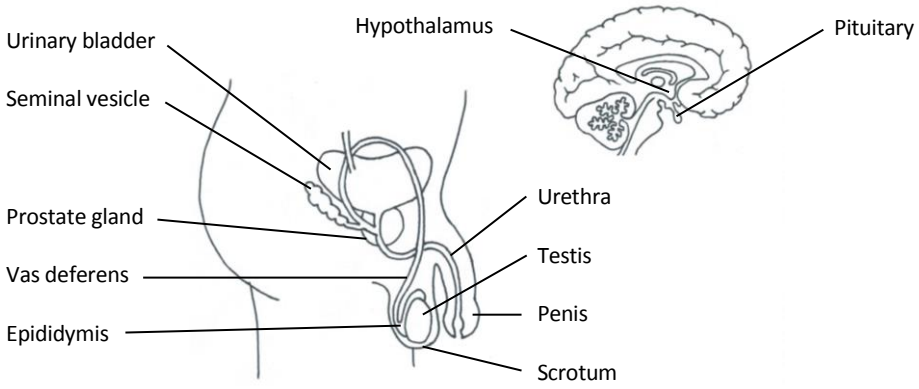

Figure 2. Illustration of the male reproductive system

The *scrotum* contains the testicles, and its primary function is to protect the testicles and maintain the slightly lower temperature which is required for normal sperm development. The *testicles* are oval structures responsible for the production of sperm and hormones. Contractions in the *epididymis* in connection with orgasm force the sperm into *vas deference* where fluids from the *seminal vesicles* and the *prostate gland* provide the sperm with important nourishment. The sperm is thereafter transported into *urethra* and the man ejaculates. Among men, the gonadal axis also plays an important role in the regulation of the reproductive system, where GnRH from the hypothalamus, LH and FSH from the pituitary gland (Figure 2) and testosterone from the testicles regulate the normal spermatogenesis. However, after puberty, the hormone levels are relatively stable compared to the female hormone cyclicity.

1.2.2.2 How do cancer and its treatment affect male fertility?

As among men, chemotherapy and radiation therapy may be toxic due to their effect on the testis cells that produce sperm. In cancer patients, the number of sperm is often reduced (oligozoospermia) or absent (azoospermia) (Rodriguez-Wallberg, 2012; Sabanegh & Ragheb, 2009). If only the later stage of the spermatogonia is affected, the disruption in sperm production may be transient, where the man can regain his fertility years after cancer treatment (Bahadur et al., 2005), but if the toxicity causes mutations in the cells that produce the sperm, permanent defects may occur (Sabanegh & Ragheb, 2009).

Surgery involving the reproductive organs (e.g. testicles or penis) or nearby systems (e.g. rectum or prostate) can, if not causing permanent infertility (e.g. in connection with bilateral orchiectomy), cause sub-fertility. Damages among men may include erectile or ejaculation dysfunction as well as oligozoospermia and azoospermia (Magelssen, Brydøy, & Fosså, 2006; Sabanegh & Ragheb, 2009). In addition, surgery or radiation therapy towards the brain may affect the gonadal axis, with following disruption of the production of testosterone.

1.2.2.3 Which fertility preservation options are available for men?

Sperm cryopreservation is an established and effective method that has been used for some decades. In some cases, especially in connection with testicular cancer and lymphoma, malignant processes may have occurred before cancer treatment, inducing oligozoospermia or azoospermia (Magelssen et al., 2006; Stahl, Stember, & Mulhall, 2012). In such cases, sperm may have to be extracted by microsurgical dissection or aspiration (Stahl et al., 2012). However, even if the sperm count is very low, it is still worthwhile to freeze them as only few vital sperm are needed to obtain viable embryos when using IVF together with intracytoplasmic sperm injection (Stahl et al., 2012). Recently, research in animal models has succeeded in *cryopreservation of testicular tissue* (stem cells) (Tournaye, Dohle, & Barratt, 2014). In the future, this may be an alternative for prepubertal boys facing sterilizing cancer treatment. The stem cells are retrieved via a testicular biopsy and cryopreserved. After treatment, stem cells can be reintroduced into the testicle, which will hopefully restart sperm production.

In connection with lymph-node dissection, or surgical treatment of cancer of the prostate, colon or bladder, *nerve-sparing techniques* can save nerve functions and thus preserve potency and ejaculatory function. In testicular cancer, fertility-sparing surgery has also been developed for treatment of early stages of the disease, and *unilateral orchiectomy* or *partial orchiectomy* may preserve fertility (Magelssen et al., 2006). When administering radiation therapy in the pelvic area, *testicular shielding* should be considered (Magelssen et al., 2006).

1.2.2.4 Fertility testing

After cancer treatment, when the man has recovered his health, a semen analysis can be done, where the quality of the semen is analysed by investigation of sperm concentration, motility and volume (Balen, 2008). As the gonadotoxic impact on sperm production can be transient and sperm production may recover years after the cancer treatment (Bahadur et al., 2005), regular fertility monitoring has been suggested (Pacey & Eiser, 2011). Fertility monitoring may help in decisions regarding the use of contraception or if there is a need for ART when the man wants to build a family.

1.3 THREATENED FERTILITY – A LITERATURE REVIEW

Clinical guidelines state that fertility-related aspects of cancer treatment should be discussed when planning treatment for patients of reproductive age (Loren et al., 2013). Receiving a cancer treatment with a possible negative impact on fertility not only involves communication about the risk of infertility and decision making regarding FP, but also the emotional aspects of living with the knowledge of possible compromised fertility. In order to investigate the psychosocial aspects of fertility-related communication, use of FP and reproductive concerns among cancer patients and survivors, a literature review was conducted.

The inclusion criteria were as follows: 1) *Population:* male and/or female cancer patients diagnosed at the age of 13 or above. 2) *Main topic:* reproductive concerns, fertility-related communication, childbearing attitudes. 3) *Design:* qualitative and quantitative. 4) *Language:* English. 5) *Date of publication:* between January 2004 and December 2014.6) *Type of publication:* Original research. The lower age restriction was based on normal puberty development among children, with the average age for first menstruation among girls and first ejaculation among boys being approximately 13 years (Moëll & Hagenäs, 2011). The restriction concerning publication date was based upon the recent developments in reproductive medicine, particularly FP options for women, which have changed compared with the FP options in the 1990s. Older papers could therefore be outdated as the conditions concerning FP differ from more recent papers.

A search of PubMed for the keywords “cancer”, “fertility”, “communication”, “information”, “infertility”, “fertility preservation” and “concerns” in different combinations, together with findings in identified papers’ reference lists, yielded 36 possible papers. Of these, five papers were excluded for the following reasons: short report based on data included and presented in another paper which were included in the review (n=2) and low methodological quality (n=3). In the end, 31 papers were included in the review (Tables 1 and 2).

1.3.1 Characteristics of included papers

In 2009, when the research project this thesis is based upon was launched, the research area was relatively unexplored. This can be seen in this literature review as of the included papers, only nine were conducted during the six-year period between 2004 and 2009. However, in the five-year period between 2010 and 2014, the number of papers in the area increased, and 22 of the included papers were conducted during that time span. This increased publication in recent years may in part be explained by the earlier mentioned developments in reproductive medicine.

Of the included papers, almost half was conducted in the US (n=11) or Canada (n=2). Other countries frequently contributing with research in the area were the UK (n=9) and Australia (n=5). None of the included papers were conducted in the Nordic countries.

Out of the 31 papers in the review (16 with quantitative design and 15 with qualitative design), 20 included only women, seven included both men and women, and four included only men. A large proportion of the papers (n=11) included only women with breast cancer. The majority of the included papers (n=19) were conducted among survivors from six month up to 15 years post diagnosis. Seven papers included both patients and survivors within days after diagnosis up to 10 years post diagnosis, and six papers included only newly diagnosed patients. About half of the papers had a focus on fertility-related communication and half on reproductive concerns; five papers included both areas. Four of the papers had a longitudinal design: Three were quantitative (two among women and one among men) following patients and/or survivors between three month up to ten years, and one was qualitative following female survivors over 12 to 18 month.

In the next section, a description of the findings of the literature review will be presented under the following headings: *Fertility-related communication*, *Reproductive concerns*, *Fertility preservation* and *Summary and conclusion of the review*.

Table 1. Selected quantitative papers (n=16)

Study	**Study design and data collection**	**Participants**		**Measures**	**Findings**
Author (year), country		No (response rate*), age and time since diagnosis	Cancer diagnoses		
Canada & Schover (2012), US	Cross sectional survey study via telephone interviews	240 women (53%), age 24-53, 6-15 years post diagnosis	Breast, cervical, Hodgkin's and non-Hodgkin's lymphoma	Reproductive concerns (RCS), infertility-specific post-traumatic symptoms measured by IES, Health-related quality of life (SF-12) and study-specific items	Unfulfilled desire to have children was significantly associated with more intrusive thoughts and avoidance (IES), and in higher levels of reproductive concerns (RCS). However, infertility was not associated with mental health (SF-12) when controlling for medical and demographic factors.
Carter et al. (2007), US	Longitudinal survey study	29 women (N/A), age 23-40, 3 and 6 month follow up after trachelectomy	Cervical	Study-specific items including one open question about specific concerns	Concerns about pregnancy increased over time and expectation of success rate about conception declined over time.
Geue et al. (2014), Germany	Cross sectional survey study	99 women and 50 men (N/A), age 19-46, 0 to >4 years post diagnosis (mean 29 month)	Breast, gynaecological, haematological, testicular, sarcoma, others	Study-specific items	Men and women rated information about fertility and children after cancer as equally important while childless rated the information as more important compared to those who already had children. More men than women used FP (56% vs. 31%).
Gorman et al. (2010), US	Longitudinal survey study, 10 year follow-up	131 women (N/A), mean age 49.1, mean 1.5 years post diagnosis,	Breast	Reproductive concerns (RCS), depressive symptoms (CES-Dsf) and study-specific items	Higher reproductive concerns were an independent predictor of consistent depressive symptoms after controlling for social support and physical health.
Gupta et al. (2013), Canada	Cross sectional survey study	94 women and 149 men (96%), age 17-35 (MD 28), within 5 years after treatment	Lymphoma, leukaemia, testicular, sarcoma and CNS	Study-specific items	Women rated information about risk of infertility and fertility preservation as more important than men (mean 9.28 vs. 8.45 in a scale from 0 to 10).
Kim et al. (2013), US	Cross sectional web-based survey study	52 women (79%), age 25-37, 5 to 10 month after FP consultation	Breast, CNS, colon, skin, haematological and gynaecological	Decisional conflict (DCS) and study-specific items	Women who 'strongly agreed' that they had opportunities to ask questions reported significantly lower decisional conflict than those who only 'agreed' (p=0.001). Those who used FP reported lower decisional conflict compare with those who did not.
Letourneau et al. (2012), US	Cross sectional survey study	1041 women (41%), mean age 40.9 (±8.4), mean time since diagnosis 9.5 years (±4.4)	Breast, leukaemia, gastrointestinal, Hodgkin's and non-Hodgkin's lymphoma	Decisional regret (DRS), quality of life (WHOQOL-BREF) and study-specific items	Women who were consulted by both oncologist and fertility specialist indicated lower decisional regret compared to women who only consulted an oncologist (p=0.001). Women who used FP reported lower decisional regret compared to those who did not (p=0.001). No significant difference in quality of life between women who used FP and those who did not.
Pacey et al. (2013), UK	Longitudinal survey study, at time of SB and one year later	91 men (87%), mean age 33.00 (SD 7.71), within day of diagnosis	Testicular and haematological	Health-related quality of life (EORTC QLQ-C30), views of clinical appointments (PMH/PSQ-MD) and study-specific items	Men who used SB were younger, more satisfied with clinic appointments and less worried about the health of future children compared to those who did not. There were no differences in health-related quality of life between men who used SB and those who did not.

Partridge et al. (2004), US	Cross sectional web-based survey study	657 women (N/A), mean age 32.9, 62% within 2 years of diagnosis (0 month to > 10 years)	Breast	Anxiety and depression (HADS) and study-specific items	More concern about infertility was associated with wish to have (additional) children, prior number of pregnancies and prior history of difficulties conceiving. There were no association between anxiety and depression and concern about infertility.
Peate et al. (2012), Australia	Prospective, longitudinal survey study	120 women (83.3%), mean age 33.2 (SD 4.3), 1 month after diagnosis and again, 12 month later	Breast	Decisional conflict (DCA), Decisional regret (DRS), anxiety and depression (HADS) and study-specific items	Women who used a decisional aid had reduced decisional conflict, decisional regret and improved knowledge of fertility-related information compared to those who received usual care.
Ruddy et al. (2014), US	Prospective survey study	620 women (N/A), age 17-40, 44 to 496 days post diagnosis	Breast	Anxiety and depression (HADS) and study-specific items	Greater concern was associated with receipt of chemotherapy, age <35 years, non-white race and not having children. Anxiety was associated with greater concerns in univariate analysis but was not significant in multivariable models.
Thewes et al. (2005), Australia	Cross sectional survey study	228 women (83%), age 20-40, 6 month to 5 years post diagnosis	Breast	Study-specific items	Women who had plans for children at diagnosis, who were childless and who prefer more information rated fertility-related information as more important.
Wenzel et al. (2005a), US	Cross sectional case-control survey study via telephone	51 women (50 controls) (81%), age 31-55, 4 to 11 years post diagnosis	Cervical	Health-related quality of life (SF-36), cancer-specific quality of life (QOL-CS) and study-specific items	Reproductive concerns were a predictor for poorer quality of life even when cancer-specific distress was taken into account.
Wenzel et al. (2005b), US	Cross sectional case-control survey	231 women (148 controls) (88%), mean age between 29.8 and 37.1 years, mean time since diagnosis between 7.2 and 8.0 years	Cervical, gestational trophoblastic disease, Hodgkin's and non-Hodgkin's lymphoma	Reproductive concerns (RCS), Health-related quality of life (SF-36), cancer-specific quality of life (QOL-CS) , cancer specific distress (IES) and study-specific items	Survivors reported more reproductive concerns compared to controls. Having more reproductive concerns was associated with poorer physical and mental health. Self-reported infertile women were more likely to report lower mental health, more cancer specific distress and overall lower physical and psychological well-being than those without fertility problems.
Yeomanson et al. (2013), UK	Cross sectional survey study	81 women and 69 men (N/A), age 14-23, at least one year post diagnosis (data collection in 2004 and 2011 in two cohorts)	Leukaemia, lymphoma, osteosarcoma, CNS, testicular, other and unknown	Study-specific items	Men more often reported having had fertility-related discussions compared to women. In addition, fertility-related discussions among men more frequently took place before start of treatment while the discussions among women more likely took place after treatment start.
Zebrack (2009), US	Cross sectional web-based survey study	635 women and 230 men (N/A), mean age 29.7 (SD 8.1), mean time since diagnosis 4.7 years (SD 4.0)	Leukaemia, breast, germ cell, sarcoma, carcinoma, CNS, thyroid, Hodgkin's and non-Hodgkin's lymphoma	Study-specific items	Younger survivors, and survivors diagnosed at a younger age reported more unmet needs. Breast cancer survivors were less likely to report unmet needs regarding infertility information.

* Response rate at the first data collection if applicable. Abbreviations: CES-Dsf, Centre for epidemiologic studies depression scale; DCA, decisional conflict aid; DCS, decisional conflict scale, DRS, decisional regret scale; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer, the current core questionnaire; FP, fertility preservation; HADS, hospital anxiety and depression scale; IES, impact on event scale; N/A, not available (study did not report); PMH/PSQ-MD, Princess Margret hospital patient satisfaction with doctor questionnaire; QOL-CS, the quality of life-cancer survivorship; RCS, the reproductive concerns scale; SB, sperm banking; SF-12, short form health survey, 12 items; SF-36, short form health survey, 36 items; WHOQOL-BREF, the brief world health organization quality of life questionnaire

Table 2. Selected qualitative papers (n=15)

Study	**Study design and data collection**	**Participants**		**Data analysis**	**Findings**
Author (year), country		No, age and time since diagnosis	Diagnosis		
Achille et al. (2006), Canada	In-depth individual interviews	20 men, age 22-47, 2-10 years post diagnosis	Testicular and Hodgkin's lymphoma	Data reduction, data display and drawing conclusions	SB presented as a part of standard care. Men who not used SB reported that they had not received any information or that the health care professionals had been unsure or unconvincing; these situations lead to regret.
Barbour et al. (2013), UK	Interviews	16 women and 14 men, age 17-39, within days or weeks following cancer diagnosis	Leukaemia, sarcoma, myeloma, CSN, ovarian, testicular, Hodgkin's and non-Hodgkin's lymphoma	Thematic analysis	The topic of FP was frequently raised for discussion with men but not with women. One third of the women who had discussed the topic of fertility had raised the issue by themselves.
Chapple et al. (2007), UK	Narrative interviews	21 men, age 16-26, combination of men being in treatment, in remission or recovered from cancer.	N/A	Thematic analysis combined with constant comparison	Men who had not been offered SB expressed regret of not have been given the choice to do so.
Connell et al. (2006), Australia	Longitudinal study, semi-structured individual interviews	13 women, age 29-40, 3 interviews over a 12-18 month period between 5-37 month post diagnosis	Breast	Data reduction, data display and drawing conclusions	Perception of fertility as an issue changed over time. For some it was constant while for others, who earlier perceived fertility as a non-issue, changed their perspective by the last interview; expressing regrets of not using FP when offered.
Corney et al. (2014a), UK	Semi-structured individual interviews	10 women, age 30-44, 8 month to 5 years post diagnosis	Breast	Framework approach	Women reported that fertility issues were generally dismissed and considered as a low priority to them.
Corney & Swinglehurst (2014b), UK	Semi-structured individual interviews	19 women, age 24-44, 6 month to 5 years post diagnosis	Breast	Thematic analysis	Women who had not been offered FP or cautioned against it did not always know why. Those who did FP were less preoccupied about their future fertility.
Eiser et al. (2011), UK	Semi-structured individual interviews	19 men, age 22-40, 5 to 13 years post SB	Testicular, leukaemia, Ewing's sarcoma, Hodgkin's and non-Hodgkin's lymphoma	Interpretive phenomenological analysis	SB was perceived as a safety net or as an assurance of a normal life after cancer. The most common reason to non-attendance to fertility monitoring was anxiety about current fertility.
Garvelink et al. (2013), Netherlands	Semi-structured individual interviews	34 women, age 22-41, mean time since fertility counselling 24 month (SD 13)	Breast, sarcoma, Hodgkin's and non-Hodgkin's lymphoma	Framework Approach	Although the women focused more on surviving most valued fertility-related information. Some women regarded fertility as a secondary issue at time of diagnosis but described how information about FP only recently had been recognised as important.

Gorman et al. (2011), US	In-depth telephone interviews	20 women, age 26-38, 1 to 13 years post diagnosis	Breast	Cross case analysis	The women felt that they had received the fertility-related information too late and that they had not had time to make informed decisions concerning FP.
Halliday et al. (2013), Australia	In-depth phenomenological interviews, face-to-face or via telephone	12 women, age 25-39, at least one year post diagnosis	Haematological	Phenomenological analysis	The women categorized themselves as different; they described themselves as not fitting or defective and misunderstood. They compared themselves with pregnant friends and the sense of 'otherness' impacted existing relationships and as well as when trying to form new relationships.
Karaöz et al. (2010), Turkey	Semi-structured individual interviews	20 women, age 21-50. Mean time since diagnosis 5.7 month (±3.3)	Breast	Thematic analysis	None of the women had received any fertility-related information. Reasons for not longer wanting children was concern about breast feeding and fear of recurrence during or after pregnancy.
Komatsu et al. (2014), Japan	Grounded theory, semi-structured individual interviews	15 women, 1 to 6 year post surgery	Cervical	Grounded theory	The core category was "FP repairs the threatened feminine identity in women with cervical cancer". The feminine identity was first threatened by the cancer and the surgery, then repaired by FP with radical trachelectomy, and finally reconstructed after the surgery.
Lee et al. (2011), UK	Ethnographic, semi-structured focus groups interviews	24 women, age 23-39, 7 to 72 month post diagnosis	Breast	Thematic analysis	The women felt that they had been denied the choice to have children or use FP by health care professionals – they had not received timely information and given the opportunity to do FP. They perceived that health care professionals had made decisions for them based on their own belief system rather than allowing the patient to decide themselves.
Peddie et al. (2012), UK	Semi-structured individual interviews	18 women and 16 men, age 17-49, during cancer treatment	Testicular, Hodgkin's and non-Hodgkin's lymphoma, leukaemia, myeloma, sarcoma, CNS, breast and ovarian	Variation of grounded theory	Almost all had received written information about risk and FP, but while all man had discussed FP few women remembered any FP discussion. Men were actively encouraged to use SB while women who had discussed FP were left feeling negative about the prospect, largely depending on how the information was presented.
Penrose et al. (2012), Australia	Semi-structured individual interviews, face-to-face or via telephone	19 women and 6 men, age 24-50, a median time of 7 month since completion of treatment	Breast, lymphoma, testicular, ovarian, germ cell and Langerhans tumour	Thematic analysis	Irrespective of desire to have children, the participants described concerns about risk of infertility as it impacted on their perceived identity or in that they would lose their ability to choose whether to have children or not.

Abbreviations: FP, fertility preservation; SB, sperm banking

1.3.2 Fertility-related communication

1.3.2.1 Attitudes towards communication

The importance of information about the risk of infertility and FP has been rated high (mean 8.77 in a scale from 0 to 10), with women giving higher rates than men (mean 9.28 vs. 8.45, p=0.03) (Gupta et al., 2013). However, another study shows no difference between male and female cancer survivors' ratings of the importance of fertility-related discussions (Geue et al., 2014). Survivors who were younger, had plans to have children at the time of diagnosis, were single or were childless were more likely to rate fertility-related discussions as important (Geue et al., 2014; Thewes, Meiser, Rickard, & Friedlander, 2003). A qualitative study indicates that the perceived importance of fertility-related communication may change over time. The women who received consultation about FP described how they had perceived fertility as a secondary issue at the time of diagnosis, but at the time of study (mean time 24 month after FP consultation), they described how they had just recently realized how important the information about FP had been (Garvelink et al., 2013).

1.3.2.2 Recall of fertility-related communication

Between 61% and 72% of female cancer survivors recalled having had fertility-related discussions sometime during treatment or follow-up (Letourneau et al., 2012; Partridge et al., 2004; Ruddy et al., 2014; Thewes et al., 2005). Two of these studies showed that many felt that their concerns had not been adequately addressed (26%) (Partridge et al., 2004) and both quantitative (Thewes et al., 2005) and qualitative studies (Barbour et al., 2013; Garvelink et al., 2013) showed that fertility-related communication with health care professionals was initiated by the women themselves. A study that evaluated the information received concerning early menopause, infertility and FP found that the women could not recall having been told about the effect of chemotherapy on their reproductive ability, nor could they recall having received any FP counselling (Karaöz et al., 2010). Studies including both male and female cancer patients/survivors found tendencies towards men more often having discussed fertility compared to women (68% vs. 56%, p=0.07 [Geue et al., 2014] and 80.3% vs. 65.2%, no test reported [Yeomanson et al., 2013]). In addition, women reported having more unmet needs about infertility information compared to men (31% vs.25%, p=<0.1, significance set at 0.1 by authors) (Zebrack, 2009). Two qualitative studies that were based on the same sample of newly diagnosed men and women showed that even though all had received written information with a brief section on FP, the topic had been frequently raised by health care professionals for discussion with men but not with women (Barbour et al., 2013; Peddie et al., 2012).

1.3.2.3 Experiences of communication

The way in which the risk of infertility and FP was communicated has been investigated to some extent. A study among women who had received FP consultation 5 to 10 months earlier showed that women who "strongly agreed" that they had opportunities to ask questions

during the consultation reported significantly lower decisional conflict regarding FP compared to those who only "agreed" with the statement (p=0.001) (Kim et al., 2013). Two other studies among female patients/survivors showed that those who used a fertility-related decisional aid (Peate et al., 2012), or consulted a reproductive specialist about fertility and FP (Letourneau et al., 2012), reported higher satisfaction with received information and lower levels of decisional conflict and decisional regrets regarding FP compared to those who had received standard care.

Having communicated about FP has been described by female survivors as a way to enable participation in choices concerning the future ability to have children (Garvelink et al., 2013). Generally, the women perceived the information as sufficient, understandable or of sufficient quantity (Garvelink et al., 2013). However, some issues had been unclear, especially concerning different aspects of FP, such as the different options and the IVF procedure. Men have also described how they did not understand how the treatment they received would impact their fertility and how they would use the banked sperm (Eiser et al., 2011). Among men, sperm banking (SB) was perceived as a part of standard care (Achille et al., 2006), and they had been actively encouraged to use SB (Peddie et al., 2012). However, men who had not used SB described how health care professionals either had appeared unsure or unconvincing, or that they had not been told about SB (Achille et al., 2006). Women who had discussed FP described how they were left feeling negative about the prospect or felt discouraged about or cautioned against it, which largely depended on how the issue was presented (Corney et al., 2014a; Corney & Swinglehurst, 2014b; Peddie et al., 2012). Not being able to recall any conversation about fertility induced negative emotions among both male and female survivors when later becoming aware of the risk (Penrose et al., 2012), and survivors expressed feeling of regret and annoyance about not being offered FP (Barbour et al., 2013; Chapple et al., 2007). Women also described how they received the information too late and that they had not had time to make informed decisions concerning FP (Gorman et al., 2011). They also felt that they had been denied the choice to have children or to use FP by health care professionals when they did not receive timely information or were not given the opportunity to do FP (Lee et al., 2011).

1.3.3 Reproductive concerns

1.3.3.1 Worry about future fertility and about having children after cancer

Between 24% and 39% of the breast cancer survivors were very concerned about becoming infertile (Partridge et al., 2004; Ruddy et al., 2014), and 11% to 29% indicated that it had impacted their cancer treatment decisions. Not surprisingly, female cancer survivors reported more reproductive concerns compared to controls without cancer experience (Wenzel et al., 2005a; Wenzel et al., 2005b). Among breast cancer survivors, predictors of higher levels of reproductive concerns were a desire to have (additional) children, fewer prior pregnancies, prior history of difficulties conceiving (Partridge et al., 2004), age <35 years, non-white race,

not having children and receipt of chemotherapy (Ruddy et al., 2014). Reproductive concerns have been shown to be associated with poorer quality of life (QoL) (Wenzel et al., 2005a; Wenzel et al., 2005b) and depressive symptoms (Gorman et al., 2010) among female cancer survivors.

Women described how infertility would impact their perceived femininity as they felt that not being able to procreate made women less attractive. This has also been shown in other studies where women described how infertility would make them less attractive to potential partners (Corney et al., 2014a; Halliday et al., 2013). A study among male survivors investigating attitudes to fertility monitoring showed that the most common reason for non-attendance to fertility monitoring was anxiety about current fertility; they preferred not knowing their fertility status before being told about sub-optimal fertility (Eiser et al., 2011). Studies show that compared to women without fertility problems, women with self-reported infertility reported worse mental health, more cancer-specific distress, lower physical and psychological well-being (Wenzel et al., 2005b) and more intrusive thoughts and emotional distress (Canada & Schover, 2012). Longitudinal studies show that experiences of fertility as an issue may change over time, with increasing levels of concerns about future pregnancies over time (Carter et al., 2007), or from describing fertility as a non-issue at the first interview to expressing regret over not having used FP when offered at the last interview (Connell et al., 2006). Female breast cancer survivors have also described other concerns beside worry of infertility, such as fear that the FP procedures would "feed the cancer" (Lee et al., 2011) and fear that a pregnancy would trigger a recurrence (Corney & Swinglehurst, 2014b; Karaöz et al., 2010; Lee et al., 2011). This fear of recurrence persisted even when the women were informed otherwise (Connell et al., 2006). Women also reported concerns about health problems in connection with pregnancy (Corney & Swinglehurst, 2014b) and about breastfeeding after breast cancer surgery (Connell et al., 2006; Karaöz et al., 2010). Also, both men and women expressed concern about future children's health and feared that they would transmit a higher risk of cancer to their children or that their children would be born with some abnormality (Achille et al., 2006; Corney & Swinglehurst, 2014b; Komatsu et al., 2014). However, one study showed that men who had banked sperm were less worried about the health of their future children compared to those who had not (Pacey et al., 2013).

1.3.4 Fertility preservation

1.3.4.1 Use of fertility preservation

Only one of the studies including both men and women reported on the use of FP, showing that more men than women used FP (56% v. 31%, p=<0.009) (Geue et al., 2014). Studies among women showed that the use of FP varied between 2% to 37% (Canada & Schover, 2012; Kim et al., 2013; Letourneau et al., 2012; Ruddy et al., 2014). The study with lowest FP use (Canada & Schover, 2012) included women diagnosed up to 15 years earlier, which according to the authors could explain the low numbers: FP at the time at their diagnosis was

not widely spread. The study reporting the highest use of FP (Kim et al., 2013) included women who all had received FP consultation. The most influential factors in the decision making about FP was the desire to have children, the amount of time needed for FP and the costs associated with it (Kim et al., 2013). Qualitative studies also found that the cost of FP could be strongly influential in the treatment decision among both men (Achille et al., 2006) and women (Garvelink et al., 2013).

1.3.4.2 Benefits of fertility preservation

Quantitative studies show that female survivors who had used FP reported lower decisional conflict (Kim et al., 2013) and decisional regret (Letourneau et al., 2012) compared to women who did not (p=0.001 respectively), and a study among men showed that men who had used SB reported higher satisfaction with clinic appointments (Pacey et al., 2013). However, there were no significant differences in QoL between patients/survivors who used FP and those who did not (Letourneau et al., 2012; Pacey et al., 2013). A qualitative study investigating fertility-related experiences among female cancer survivors reported that women who had been able to freeze oocytes or embryos were much less preoccupied about their future fertility compared to those who had not (Corney & Swinglehurst, 2014b). In a qualitative study among male survivors who all had banked sperm, the men described how SB had provided a safety net that ensured them the possibility of having a "normal life" after cancer treatment (Eiser et al., 2011). A grounded theory study among women treated for cervical cancer that underwent FP surgery described how the radical trachelectomy was a way to repair and reconstruct the threatened feminine identity; the wish to maintain fertility was not only connected with desire to have children but to the significant meaning of being a woman (Komatsu et al., 2014).

1.3.5 Summary and conclusion of the review

The literature review showed that even though men and women diagnosed with cancer feel positively towards fertility-related communication, many report a lack of fertility-related communication, especially women. Having received treatment with a possible negative impact on fertility created concerns among both men and women, and the factors identified as being associated with greater concerns were younger age and not having children—two elements usually connected to a desire to have children sometime in the future. Use of FP was associated with less decisional conflicts and regrets, and FP was experienced as a way to achieve restore "normality". The research indicates sex differences; it seems that men more often can recall having had fertility-related communication with health care professionals compared to women. Whilst men experienced FP as a part of cancer care and were encouraged to bank sperm, women felt discouraged depending on the way in which FP was presented to them. Women also seemed to have more concerns, as the besides worry about infertility, also had concerns about future pregnancies. The literature review also indicated that patients and survivors' experiences of fertility change over time.

It seems as the experience of threatened fertility, to a large extent, is influenced by how the issue is communicated; lack of information, unanswered questions and non-responsiveness from health care professionals created concerns among both men and women.

1.4 THEORETICAL FRAMEWORK

Communication plays a large part in the care of patients, and extensive research has been conducted to investigate the different aspects of communication in health care. In his concept analysis of communication in caring (Fredriksson, 2012), Fredriksson found that there were two discernible traditions in the literature with different underlying assumptions: the dualistic-reductionist tradition and the holistic-humanistic tradition. In the first, the assumption is that communication is linear, with a sender who "codes" thoughts into words and a receiver who "decodes" the words back to the original thoughts communicated by the sender. Research in this area is often oriented towards studying the measurable qualities of communication or to measure outcomes of communication interventions. In the holistic-humanistic tradition, the assumption is that communication is a mutually interpretive and problem-solving process. Communication is seen as complex; research focuses on the relationship between the carer and patient, and theory tries to embrace the complexity in the interpersonal relations.

In the review of the literature on the aspects of threatened fertility, one can discern both traditions in how to investigate fertility-related communication among cancer patients and survivors. However, findings indicate that experiences of fertility-related communication and the risk of infertility are not only dependent upon the facts given in the communication but also in how the person interprets the information received. One model that takes into account the complexity of health care communication is the patient–professional communication framework (Feldman-Stewart, Brundage, & Tishelman, 2005).

1.4.1 The patient–professional communication framework

The patient–professional communication framework (Feldman-Stewart et al., 2005), developed on earlier classic models of communication have been used in developing interventions, organizes findings in reviews and in clinical studies (Brundage, Feldman-Stewart, & Tishelman, 2010; Carlson, Feldman-Stewart, Tishelman, Brundage, & Team, 2005; Jangland, Gunningberg, & Carlsson, 2009; Parker, Davison, Tishelman, Brundage, & Team, 2005). The model focuses foremost on the one-to-one, in-person communication and addresses both the patients and the professionals' goals (Figure 3). Communication, which is extended over time, is dependent on the participants' attributes and involves both the conveying and receiving of messages. The model also takes into account that the communication process takes place within an environmental context. The framework consists of four components: G*oals*, *Attributes*, *Communication process* and *Environment.*

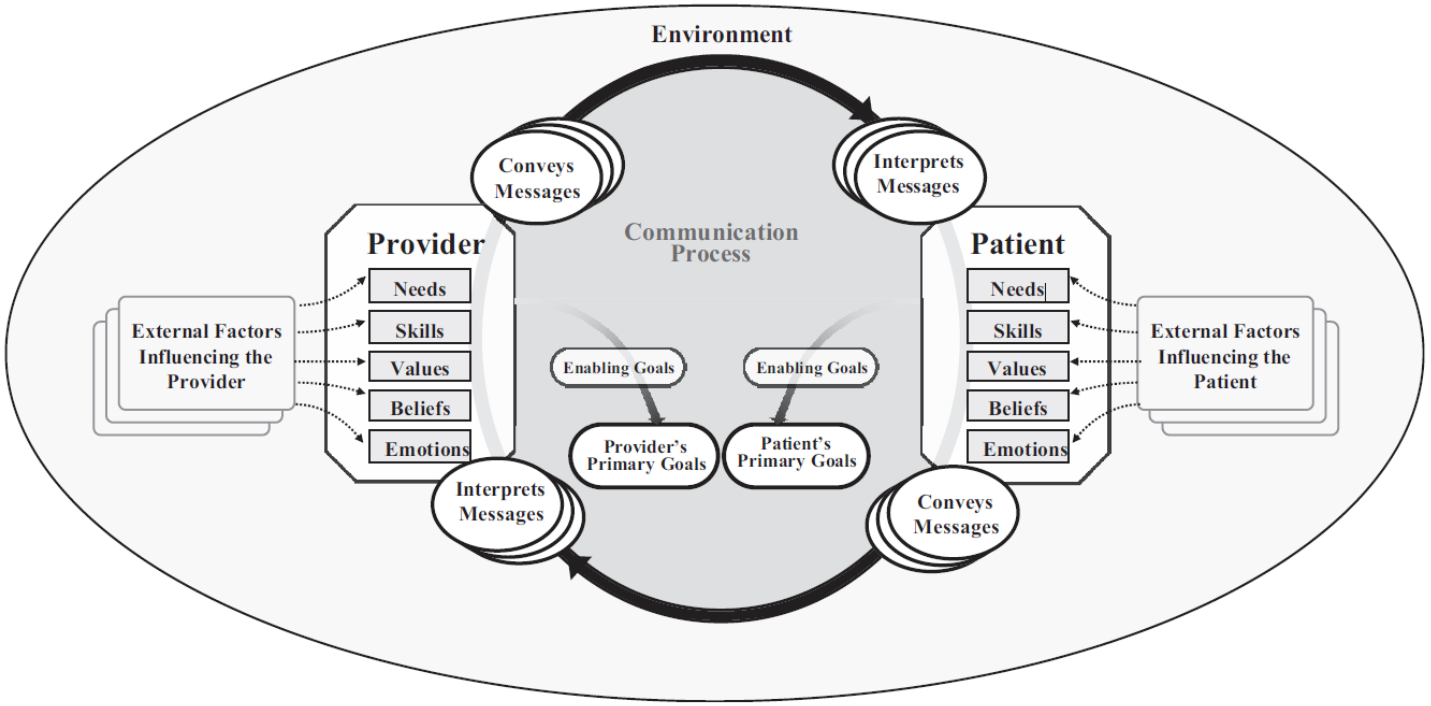

Figure 3. The patient-professional communication framework (Feldman-Stewart et al., 2005)

1.4.1.1 Goals

Goals are defined as "the objective of the participants' communication effort", and each encounter has at least one goal based on participants' needs, for example, to obtain knowledge about patients' symptoms or to learn more about the received diagnosis. It is not always that the participants have articulated goals in a communication encounter, especially in situations with great emotional distress. It is also possible that the goals between or within participants' are in conflict with each other, which may impede fruitful communication. The framework defines *primary goals* and *enabling goals*. Primary goals are the goals that catalyse the communication, the reasons why the communication was initiated, while enabling goals are steps that facilitate in reaching the primary goals. For example, professionals' questions about patients' reproductive desire may be an enabling goal to reach the primary goal, that is, to decide which treatment to choose.

1.4.1.2 Attributes

Each participant's attributes affect the content and form of the communication. The framework has conceptualized five attributes: *needs*, *beliefs*, *values*, *skills* and *emotions.* The participants' needs are what motivate them. The needs can be at all levels, from basic physiological needs (e.g. food or air) to more complex needs, such as self-actualization needs (e.g. need of control or need to not be judged). Beliefs are the participants' understanding of the world and what is happening around them, for example the cancer patient's understanding of what an early menopause may mean. Beliefs are the attributes which are most likely to be altered in communication when new knowledge is added. Values include principles or standards that are fundamental to the participants' functioning. Skills are the participants' ability to reach their communicative goals, such as professionals' skills in conveying knowledge about how cancer treatment affects the fertility, but also to interpret received messages. Emotions include both negative and positive emotions, which can influence communication, for example, the shock of having been diagnosed with cancer.

1.4.1.3 Communication process

The heart and centre of the framework is the provision and interpretation of messages. Messages can be conveyed intentionally or unintentionally, and several messages can be conveyed and received at the same time. The framework distinguishes between three types of messages: two active, *verbal* and *non-verbal*, and one passive, *silence*. Verbal refers to communication using words, while the non-verbal refers to body language, tone of voice and facial expressions. The framework highlights the importance of silence in the communication process, giving time for reflection and recuperation. Silence can also be explicit, when participants choose to not answer a question, or implicit, when participants avoid a topic. The communication process spans over time; messages are conveyed and received and may be influenced by communication that occurred in the past, which in turn impacts future communication.

1.4.1.4 Environment

The last component of the framework is the environment. The environment contains not only the physical setting in which communication occurs, but also its social, cultural, legal and physical aspects, which can all impact the communication process by influencing the participants' attributes. An example of such environmental influence could be if there are clear guidelines in how to refer to patients who need to undergo FP. This influences values and beliefs, which may lead health care professionals to, by word or by tone of voice, encourage patients to pursue FP.

1.5 THE HEALTH CARE CONTEXT

The health care systems in the Nordic countries are tax-funded, with a high proportion of public health care professionals. In Sweden, health care is tax-funded by 80%. The level of self-financing are determined by individual county councils and municipalities and the residents pay about 17% of the cost, which is charged in connection with visits to health care, hospitalization and purchase of medicines. Only 4% of the population has private health insurance (Anell, Glenngard, & Merkur, 2012). There is an upper limit to self-financing, the so-called high-cost protection (högkostnadsskyddet). When the costs of pharmaceuticals or health care visits exceed a certain sum within a year, the high-cost protection activates and for the remainder of the 12-month period, the residents do not have to pay any charges. An individual resident never pay more than SEK 1,100 (€122) for health care visits within a period of 12 months and SEK 2,200 (€244) for prescribed drugs (Anell et al., 2012). This system lays the base to an equitable health care system where the residents have the same opportunity to receive good health care. In Sweden, men and women diagnosed with cancer and facing a treatment with a possible negative impact on fertility have the right to use FP options without any costs. After cancer treatment, and if the cancer survivors have fertility problems and do not already have children, the survivors have the right to tax-funded infertility treatment. If they already have children, the survivors have to fund the infertility treatment themselves.

2 RATIONALE

Many men and women face the risk of compromised fertility when they want to start or complete their intended family after cancer treatment. Most of the studies investigating fertility-related communication and experiences of fertility after cancer have been conducted among female cancer patients and survivors, and there is limited knowledge about the experiences among men. As earlier research points towards sex differences, studies including both men and women may contribute important knowledge about different aspects of fertility-related communication and reproductive concerns. No qualitative study was found that investigated the experiences of the risk of infertility among newly diagnosed cancer patients. Also, as longitudinal and retrospective studies indicate that the experience of risk of infertility may change over time, longitudinal studies including men and women undergoing initial cancer treatment may contribute with new insights into how the issue of fertility after cancer impacts men and women's lives. Earlier research shows that both male and female cancer survivors regard the costs of FP as an important factor when deciding whether to use FP or not. In Sweden, FP is available to cancer patients as a part of the tax-funded health care system. As the bulk of research has been conducted in the US, and no studies have been found investigating the issue in the Nordic countries, a study in the Swedish health care context may contribute to new knowledge. Through increased knowledge about how men and women's experiences of risk of infertility as well as their experiences of communication about the risk of infertility and FP, health care professionals can gain a better understanding of the complex situation arising from receiving lifesaving cancer treatment that may affect future fertility.

3 AIMS

The overall aim of this thesis was to study the perceptions and experiences of fertility-related communication among men and women of reproductive age diagnosed with cancer in Sweden. An additional aim was to investigate the experiences of receiving treatment with a potential negative impact on fertility and how this is experienced over time.

PAPER I

The aim was twofold: to investigate cancer survivors' perception of fertility-related information and use of FP options in connection with cancer treatment during reproductive age, and to investigate the relationships between receiving fertility-related information and socio-demographic factors, diagnosis and a pre-treatment desire for children.

PAPER II

The aim was to investigate desire for children, difficulties achieving a pregnancy and infertility distress among survivors three to seven years after cancer treatment in reproductive age.

PAPER III

The aim was to investigate newly diagnosed cancer patients' experiences of fertility-related communication and their reasoning about the risk of future infertility.

.**PAPER IV**

The aim was to explore how men and women experience life with regard to fertility and having children over the first two years following a cancer diagnosis.

4 METHODS

4.1 DESIGN

The thesis is based on two studies: a large population-based retrospective survey study and a longitudinal interview study. An overview of both studies and the subsequent papers is presented in Table 3.

Table 3. Overview of the general design of the project

Study	Design	Data collection	Participants	Paper	Analysis
1	Cross-sectional survey study	Study-specific items, SF-36, FPI	484 cancer survivors (328 women and 156 men)	I	Logistic regression and χ^2 test
				II	Logistic regression , *t*-test and χ^2 test
2	Longitudinal interview study	Individual semi-structured interviews	Interview 1: 11 women and 10 men	III	Qualitative content analysis
			Interview 2: 9 women and 7 men	IV	Qualitative content analysis with focus on stability or change over time

4.2 STUDY 1 – A CROSS SECTIONAL SURVEY STUDY

4.2.1 Participants

Possible participants were men and women diagnosed with cancer in the Uppsala/Örebro region in Sweden, which includes a population of approximately two million people. The inclusion criteria was as follows: being diagnosed between 2003 and 2007 at the age of 18–45 with lymphoma (Hodgkin's and non-Hodgkin's), acute leukaemia (acute lymphatic leukaemia and acute myeloid leukaemia), testicular cancer, ovarian cancer or breast cancer requiring chemotherapy treatment. The selected diagnoses were chosen as they typically require treatment with a negative impact on fertility. The age interval was based upon statistics regarding the ages at which most women in Sweden give birth (Statistics Sweden, 2010); the same age span was chosen for the men in order to avoid other confounding factors, such as age-related differences in health that could have an impact on analysis.

4.2.2 Procedure

In 2010, a total of 494 women and 316 men who met the inclusion criteria were identified from the Swedish Cancer Registry and selected Quality Cancer Registers. The possible participants were sent a letter of invitation outlining the study aim and a postal survey. A maximum of two reminders were sent to non-respondents. A completed survey was considered as informed consent.

4.2.3 Data collection

The survey included study-specific items and two validated instruments, the Swedish version of Short-Form 36 Health Survey (SF-36) and the Fertility Problem Inventory (FPI). The study-specific items were developed on the bases on earlier research and clinical experience. A pilot study, which included a sub-set of questions measuring participants' perception of partaking in the study (Kreicbergs, Valdimarsdottir, Steineck, & Henter, 2004), conducted among 66 female cancer survivors confirmed the face validity and feasibility of the study. Data obtained in the pilot study were included in the analysis.

4.2.3.1 Fertility-related communication and use of fertility preservation

Oncologists or haematologists are primarily responsible for discussing the potential side effects of cancer treatment with their patients. Therefore, the items assessing perception of fertility-related communication were formulated to measure recalled communication with these professionals when primary treatment was planned.

Communication about the risk of infertility was assessed with following items: If they had talked with their physician about the treatments impact on fertility (Yes/No/Do not remember), if yes, at what time point they had received the information (Before start of treatment/After start of treatment), how the information was provided (Orally/Written material/Personal notes) and, depending on sex, the level of risk for amenorrhea, reduced ability to become pregnant, premature menopause, decreased sperm production and problems with erection and ejaculation (No risk/Some risk/High risk/Do not remember).

Communication about FP was assessed with following items: If they had talked with their physician about FP (Yes/No/Do not remember), if yes and depending on sex, which FP options had been discussed (Cryopreservation of embryo, oocytes, ovarian tissue or sperm/Treatment with GnRH agonists/Radiation shielding of gonads) and how the information was provided (Orally/Written material/Personal notes). They were also asked to indicate whether they had used any FP (Yes/No), and if no, they were also asked to indicate why in an open-ended format.

4.2.3.2 Mental health

To measure mental health, the Swedish version of Short-Form 36 Health Survey (SF-36) was used. The 36 items in SF-36 forms eight scales: Physical Functioning (PF), Role-Physical

(RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE) and Mental Health (MH). Responses are given on Likert scale and vary between two to six choices. The raw scores for each question are coded, summed and transformed into a scale from 0 (worst possible health) to 100 (best possible health). Based on the eight scales, two summary index scores are formed indicating physical health (Physical Component Summary, PCS) and mental health (Mental Component Summary, MCS) (Ware & Kosinski, 2001). The later SF-36 MCS was used in this study.

The validity of the instrument was established earlier through an examination of criterion-based validity, showing that groups with or without different health conditions scored in expected directions, and construct validity, where MCS and PCS explained 73% of the variance and together they accounted for at least two-thirds of the variance in each scale (Taft, Karlsson, & Sullivan, 2004). The internal consistency in the eight scales has been reported to be moderate to high (Cronbach's α 0.79 to 0.93) (Sullivan, Karlsson, & Ware, 1995).

4.2.3.3 Infertility-related stress

In order to measure infertility-related stress, the Fertility Problem Inventory (FPI) was used (Newton, Sherrard, & Glavac, 1999). The instrument was originally developed to measure infertility-related stress among men and women undergoing infertility treatment. The 46 items forms five subscales: Need for Parenthood, Rejection of Childfree Lifestyle, Sexual Concern, Social Concern and Relationship Concern. Responses are given on a Likert scale with six choices from Strongly agree (1) to Strongly disagree (6). For the purpose of the study, a seventh response alternative was added: "Not applicable". The scores for each question in the subscales are summed, where a higher value indicates higher infertility-related stress. By summing the scores obtained in the five subscales, a composite scale ranging from 46 to 276 indicates Global stress. An examination of the factor structure of the FPI with confirmatory analysis (Moura-Ramos, Gameiro, Canavarro, & Soares, 2012) suggested a two-dimension solution of the five sub-themes: 1) Representations about the Importance of Parenthood (FPI-dimension RIP), in which the subscales Need for Parenthood and Rejection of Childfree Lifestyle are included, and 2) Impact on Life Domains (FPI-dimension ILD), in which the subscales Sexual Concern, Social Concern and Relationship Concern are included. All participants were asked to respond to questions in FPI-dimension RIP, and participants with self-reported ongoing fertility problems were also asked to respond to the questions in FPI-dimension ILD. The FPI was translated into Swedish for this study using independent forward and backward translations (Sousa & Rojjanasrirat, 2011) by professional translators with Swedish and English as their first language, respectively.

The validity of the instrument was established earlier through an examination of discriminant validity, showing that the subscales measured separate but related dimensions of stress, and convergent validity, showing that correlations between FPI subscales and standardized measures were in expected directions and moderate in size. The internal consistency of the

five subscales has been shown to be moderate to high (Cronbach's α 0.77 to o.93) (Newton et al., 1999).

4.2.3.4 Behavioural intentions in case of infertility

To measure behavioural intentions in the case of infertility, the participants were asked to indicate on VAS the likelihood of using IVF, using donated sperm or oocytes or adopting (endpoints 0 cm, Entirely unlikely and 10 cm, Highly likely). The scales have been used in earlier research (Lampic, Svanberg, Karlström, & Tyden, 2006).

4.2.3.5 Socio-demographic and reproductive variables

The survey also assessed the following clinical and socio-demographic variables: cancer diagnosis and treatment, sex, age, educational level, marital status, menopause status, children born before and after the cancer treatment, pre-treatment desire to have (additional) children, desire to have (additional) children at the time of study and post-treatment fertility problems.

4.2.4 Analysis

Statistical analyses were performed using PASW Statistics 19, 20 and 22 (SPSS Inc., Chicago, IL), and all tests were two tailed. A level of $p \leq 0.05$ was used to indicate statistical significance.

4.2.4.1 Paper I

Comparisons between groups within single items were assessed with a Chi square test. By using multiple logistic regression, the relationships between patient characteristics (sex, age at diagnosis dichotomized as ≤35 and >35, children at diagnosis, diagnosis and pre-treatment desire for children), recall of having communicated about risk of infertility and FP (dichotomized as Yes or No/Do not know) and use of FP (Yes or No) were investigated. Variables significant in univariate analysis were entered into three different models: two separated by sex and one for the total sample.

4.2.4.2 Paper II

Differences between groups were assessed by using a Chi square test or *t*-test. Multiple logistic regression was used to investigate the relationships between patient characteristics (sex, age at time of study dichotomized as ≤35 and >35, children at the time of diagnosis and children born after diagnosis) and the desire to have children at the time of study (dichotomised as Definite desire/Possible desire or No desire). All variables were entered into two different models: one for those who recalled having no pre-treatment desire to have children and one for those who recalled having a pre-treatment desire to have children. In the analysis concerning fertility problems, only women aged ≤ 40 were included.

4.3 STUDY 2 – A LONGITUDINAL INTERVIEW STUDY

4.3.1 Participants

Between June 2009 and May 2011, possible participants were approached about study participation. Inclusion criteria were being aged between 20 and 45 years, having recently being diagnosed with cancer, being scheduled to undergo a curative cancer treatment with a possible negative impact on fertility and being able to communicate in Swedish. The possible participants were identified by designated personnel or by the author of this thesis at three cancer wards specialized in haematology and/or oncology at a university hospital in Sweden.

4.3.2 Procedure

A letter of invitation provided information about the study's aim, stating that two interviews were planned over two years and that any participation would be voluntary and could be interrupted at any time. Twenty-nine men and women met the inclusion criteria, and 11 women and 10 men chose to participate in the first interview (Figure 4). Two years after the first interview, between August 2011 and May 2013, the surviving participants were contacted by mail for participation in a second interview, and nine women and seven men chose to participate. All participants signed a consent form before the interviews.

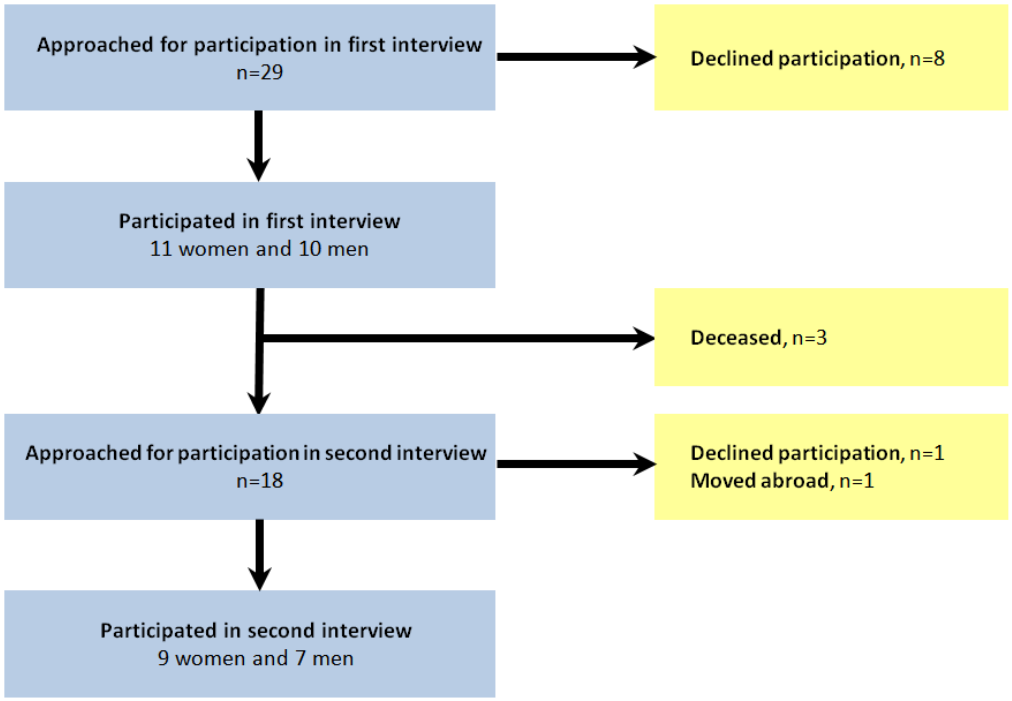

Figure 4. Flow-chart of participants in the longitudinal interview study among men and women newly diagnosed with cancer

4.3.3 Data collection

Data were collected using individual semi-structured interviews focusing on the area of fertility in connection with cancer treatment. The author of this thesis, who did not participate in the care of the participants, conducted all the interviews. The first interviews took place at the hospital during the participants' initial cancer treatment at the average of 8.5 weeks following cancer diagnosis (range 2 days to 12 weeks). These interviews focused on experiences of fertility-related communication, decision making regarding FP and feelings about the risk for infertility. The second interviews occurred two years later and were mostly conducted in the participants' homes. These interviews focused on experiences of having received treatment with a potential negative impact on fertility and thoughts about having children after cancer. In order to enrich and clarify the narratives, supplementary questions were asked, such as "What do you mean when you say...?", "How did you feel about that?" or "What happened then?" In some cases, at the request of the participant, partners were present at the interviews (three at the first interview and two at the second interview); however, partners' comments were not included in the analysis. The first interviews lasted between 15 and 51 minutes (median 25 minutes), and the second interviews took between 26 and 86 minutes (median 47 minutes).All interviews were digitally recorded and transcribed verbatim.

4.3.4 Analysis

Qualitative content analysis was used as described by Graneheim and Lundman (2004). In their description of qualitative content analysis the underlying assumption is that "reality can be interpreted in various ways and the understanding is dependent on subjective interpretation" (Graneheim & Lundman, 2004). Therefore texts, such as a transcribed interview, always are interpreted to some degree. However, the interpretation may vary in both depth and level of abstraction. The manifest content of the text is the descriptive level of the text, presented as categories and sub-categories – answering the question 'What? The latent content is the interpreted underlying meaning through categories and sub-categories, which is presented as themes and sub-themes – answering the question 'How? (Graneheim & Lundman, 2004). As the research area was relatively unexplored an inductive analysis process was used where the analysis is data driven (Elo & Kyngäs, 2008). However, as a deductive approach is useful when comparing data from different time-points (Elo & Kyngäs, 2008), deductive analysis process was used as a part in the analysis in Paper IV.

The analysis was primarily performed by GA, but the research team continuously discussed the analysis process, including the identified meaning units, the categorization and abstraction. As the quantity of data was large, especially in the analysis for Paper IV, the software program NVivo, version 10 (QSR International), was used to assist in the organization of data during the analysis.

4.3.4.1 Paper III

A structured analysis was carried out in six steps, with the help of techniques described by Graneheim and Lundman (2004): 1) The transcripts were read to get a sense of the participants' story. 2) Meaning units consisting of single words, sentences or whole paragraphs related to the study aim were identified. 3) The meaning units were condensed to shorten the text while retaining its content. 4) Each condensed meaning unit was given a code that mirrored its content. 5) The codes were then compared and grouped into sub-categories and categories reflecting the same topic. 6) Based on the interpretation of the meaning in the categories, three sub-themes and one main theme were formed.

4.3.4.2 Paper IV

Paper IV was based on two interviews spaced two years apart. One of the main purposes of qualitative longitudinal studies is to capture experiences through time in order to identify patterns of change, or stability, over time (Saldaña, 2003). There is no universal method for analysing longitudinal qualitative data, instead the way in how to handle the data depends on the context, and relies on the artistry of the analyst (Saldaña, 2003). To address the study aim, to explore experiences over time, a strategy was formed specifically for the paper which resulted in data being analysed in three phases.

Phase 1 Each participant's two interviews were condensed into short narratives focusing on how the participant experienced life with regard to fertility and having children after cancer through time. Narratives that displayed the same patterns were then brought together, and four groups were formed. These groups contained four patterns reflecting different experiences through time, which gave a first understanding of the data. This analysis was then laid aside.

Phase 2 Each participant's two transcribed interviews were analysed separately in two steps by qualitative content analysis. In Step 1, an inductive structured analysis of the first interview was carried out as earlier described in Study III (Graneheim & Lundman, 2004). In Step 2, by using same structured analysis, a deductive analysis of the second interview was done. Identified codes from the second interview were grouped into already existing categories from the inductive analysis in Step 1, and codes not fitting into already existing codes formed new categories. This structured analysis of each participant's interviews enabled a closer examination of the experiences through time on the individual level. By studying the identified categories, if and when they appeared or disappeared over time and where the emphasis laid in the categories, the participants' patterns of experience through time could be distinguished. Participants who displayed the same patterns of experience were then grouped together. The grouping obtained by this structured analysis was then compared with the grouping obtained in Phase 1. While structured analysis in Phase 2 for the most part confirmed the first understanding in Phase 1, two participants were relocated to a different group that better corresponded with their experiences through time.

Phase 3 While still remaining position of being from first or second interview, data from participants in the same group were brought together, and categories reflecting same topic were merged. Through this procedure, patterns of experience distinctive to the four different groups could more clearly discerned and formulated.

5 ETHICAL CONSIDERATIONS

All procedures were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000. Study 1 was approved by the Regional Ethical Review Board in Stockholm, Sweden (nr: 2010/195-31/4), and Study 2 by the Regional Ethical Review Board in Uppsala, Sweden (nr: 2009/136). The project has followed the three fundamental ethical principles: *The principal of beneficence*, *The principal of respect for human dignity* and *The principal of justice* (Polit & Beck, 2004).

The principal of beneficence According to the Health and Medical Service Act (1982:763), in the Swedish law, a patient must be given individualized information regarding his/her state of health and the treatment methods available. In Sweden, there is no legal obligation to communicate the risk of infertility and FP options to patients; however guidelines recommend that this information should be provided to all men and women of reproductive age scheduled to receive cancer treatment (Loren et al., 2013). Given that earlier research indicated that relatively large groups of men and women do not recall receiving any fertility-related communications, and that fertility can be a sensitive issue, special care was taken in the planning of the studies. Ethical aspects were discussed, and the risk of upsetting cancer patients and survivors who had not had any discussions about the fertility-related aspects of cancer treatment was carefully balanced with the benefit of gaining knowledge about what fertility-related communication young adult cancer patients receive. In Study 1, a pilot study was performed, which included a sub-set of questions measuring survivors' perceptions of participating in the study. These questions had been previously used to assess the ethical aspects of contacting parents of children who had died of cancer (Kreicbergs et al., 2004). Of the 66 respondents in the pilot study, a majority stated that it was rather or very valuable to conduct such a survey. However, four respondents indicated negative effects from participation in the survey and felt a need to contact the research group or the hospital where they were treated. Before start of Study 1, all operation managers at the clinics in the region were contacted about the study and prepared to meet any fertility-related questions from men and women receiving the survey. In Study 2, the interviewer allocated extra time after the interview to detect any distress, and where when needed, encouraged the participants to talk with their oncologist or haematologist about the matter.

The principal of respect for human dignity All participants received written information about the study. In Study 1, returning a completed survey was regarded as providing informed consent, and in Study 2 a consent form was obtained before the first interview.

The principal of justice All men and women approached for participation in the studies were informed that any participation would be voluntary, and in Study 2, they were also informed that participation or non-participation would not affect their care and treatment.

6 RESULTS

6.1 STUDY 1

6.1.1 Participants

Out of the 810 cancer survivors who met the inclusion criteria, seven had unknown addresses and could not be contacted. Of the 803 contacted survivors, 328 women and 156 men chose to participate, yielding a response rate of 60%. Analysis of the non-responders showed that more women (67%) than men (50%) chose to participate (χ^2=22.977, df=1, p<0.001). No other differences could be found between responders and non-responders. Socio-demographic and clinical characteristics are presented in Table 4. Women were older and had more often children at the time of diagnosis. Men had more often had children after the cancer diagnosis compared to women. Mean age at the time of study was 41.2 years (median 42; range 21–53) and the median time since diagnosis was 5.0 years (median, 5.0; range 3–7). Two of the women reported that they were in menopause at the time of diagnosis and ten were unsure.

Table 4. Socio-demographic and clinical characteristics of participants

Characteristics	**Total** (n=484)	**Men** (n=156)	**Women** (n=328)	
	Mean (SD)	Mean (SD)	Mean (SD)	*p*
Age at time of study	41.2 (7.4)	37.8 (7.2)	42.8 (6.9)	<0.001[d]
Time since diagnosis	5.0 (1.4)	4.9 (1.4)	5.0 (1.4)	NS
	No.(%)	No.(%)	No.(%)	
Diagnosis				
Breast cancer	245 (50.6)	-	245 (74.7)	-
Ovarian cancer	17 (3.5)	-	17 (5.2)	-
Lymphoma	85 (17.6)	35 (22.4)	50 (15.2)	NS
Leukemia	26 (5.4)	10 (6.4)	16 (4.9)	NS
Testicular cancer	111 (22.9)	111 (71.2)	-	-
Marital status at time of study				NS
Living alone	95 (19.6)	31 (19.9)	64 (19.5)	
Married/Cohabiting	389 (80.4)	125 (80.1)	264 (80.5)	
Educational level at time of study[a]				NS[e]
Compulsory school[b]	37 (7.6)	6 (3.8)	31 (9.5)	
Secondary education[c]	265 (54.8)	99 (63.5)	166 (50.9)	
University education	180 (37.2)	51 (32.7)	129 (39.6)	
Children at diagnosis	337 (69.6)	77 (49.4)	260 (79.3)	<0.001[f]
Children born after diagnosis	60 (12.4)	36 (23.0)	24 (7.3)	<0.001[f]

[a] Two women did not answer the question; [b] Nine years of education, 7–15 years of age; [c] Two to four years of education after compulsory school; [d] Between sex, 2-tailed *t*-test; [e] Between sex: University vs. Non-university education, 2-tailed χ^2 test; [f] Between sex, 2-tailed χ^2 test.

6.1.2 Paper I – Main findings

The aim was twofold: to investigate cancer survivors' perception of fertility-related information and use of FP options in connection with cancer treatment during reproductive age, and to investigate the relationships between receiving fertility-related information and socio-demographic factors, diagnosis and a pre-treatment desire for children.

6.1.2.1 Communication about the impact of cancer treatment on fertility

More men than women reported having had fertility-related discussions about the possible impact of cancer treatment on their fertility (n=125, 80% vs. n=158, 48%; χ^2= 45.75, df=1, p<0.001) and multiple logistic regression analysis showed that men were more than three times likely to report such discussions as women were (OR 3.15, 95% CI 1.93-5.15). Others predictors were a pre-treatment desire to have children (OR 3.48, 95% CI 1.20-6.05) and being ≤ 35 year at diagnosis (OR 1.98, 95% CI 1.20-3.27). The recalled level of risk of fertility problems among the 158 women and 125 men who reported having received information about the treatment's potential impact on fertility is presented in Table 5.

Table 5. Recalled risk assessment about the treatment's potential impact on fertility*

	Women (n=158)			**Men** (n=125)		
	Amenorrhea	Reduced ability to become pregnant	Premature menopause	Decreased sperm count	Erectile dysfunction	Ejaculation problems
	No.(%)	No.(%)	No.(%)	No.(%)	No.(%)	No.(%)
No risk	9 (5.8)	7 (4.5)	6 (3.9)	6 (4.8)	41 (33.1)	43 (34.4)
Some risk	63 (41.2)	50 (31.8)	43 (28.1)	71 (56.8)	30 (24.2)	18 (14.4)
High risk	65 (42.5)	75 (47.8)	69 (45.1)	39 (31.2)	3 (2.4)	4 (3.2)
Do not remember/ Did not receive any information	16 (10.5)	25 (15.9)	35 (22.9)	9 (7.2)	50 (40.3)	60 (48.0)

* Some did not indicate any of the options, or not all options

6.1.2.2 Communication about and use of fertility preservation

Men recalled having discussed FP more often than women (n=106, 68% vs. n=45, 14%; χ^2=146.38, df=1, p<0.001), and the multiple logistic regression analysis showed that men were 14 times more likely having communicated about FP options compared to women (OR 14.42, 95% CI 7.13-29.16). Other predictors were being ≤ 35 year at diagnosis (OR 5.05, 95% CI 2.44-10.46) and having no children at diagnosis (OR 2.50, 95% CI 1.20-5.22). More than half of the men (n=85, 54%) cryopreserved sperm. Out of these men, 29 reported that they had no desire to have children when they banked sperm. Eleven of the women reported

that they had attempted do FP, but in three cases, the attempt had been unsuccessful, and in one case, the stimulation was terminated as the cancer treatment had to be started. The remaining seven women cryopreserved oocytes and/or embryos (n=5) or used ovarian suppression with GnRH agonists (n=2).

6.1.3 Paper II – Main findings

The aim was to investigate desire for children, difficulties achieving a pregnancy and infertility distress among survivors three to seven years after cancer treatment in reproductive age.

6.1.3.1 Desire for children

Of the 83 men and 246 women who recalled having no pre-treatment desire to have children, the majority (83%) kept this view three to seven years after diagnosis. Multiple logistic regression analysis showed that not having children at the time of diagnosis was the single most important predictor (OR 34.69, 95% CI 3.87-311.41) for changing to a definite or possible desire to have children, followed by being ≤ 35 year at time of study (OR 14.74, 95% CI 3.24-67.09). In this group, 65.5% of the men had used FP, while none of the women had done so.

Out of the 71 men and 81 women of the participants who recalled having had a pre-treatment desire to have children, the majority (78%) still had a definite or possible desire to have children three to seven years later. Multiple logistic regression analysis showed that having had children after the cancer diagnosis was the most important predictor (OR 4.79, 95% CI 2.05-11.20) for no longer wanting children, followed by already having children at the time of diagnosis (OR 4.01, 95% CI 1.77-9.12) and being >35 years at time of study (OR 2.77, 95% CI 1.26-6.10).

6.1.3.2 Unfulfilled desire to have children and mental health

Among the participants who recalled having a pre-treatment desire to have children, those who had not had children after diagnosis reported lower levels of mental health (SF-36 MCS) compared to those who had children after their cancer diagnosis (mean=43.03 vs. mean=47.76, t=2.28, df=145, p=0.024).

6.1.3.3 Fertility problems after cancer treatment

After excluding women aged over 40, a total of 83 participants continued to have a desire to have children at the time of study. Almost one-third of this group (n=26) reported having had experienced fertility problems after cancer treatment, and 19 of these indicated that they had ongoing problems. The men and women who reported ongoing fertility problems were asked to indicate their level of infertility-related on FPI, and the results are presented in Table 6.

Table 6. Infertility-related stress among survivors with ongoing fertility problems

Infertility-related stress by Fertility Problem Inventory (FPI)[a]	**Women** (n=7)	**Men** (n=12)
	Mean(SD)	Mean(SD)
Global Stress	178.2(43.2)	125.6(24.3)
FPI-dimension RIP[b]	76.7(18.4)	64.7(9.3)
Rejection of Childfree Lifestyle	32.8(7.9)	27.9(3.9)
Need for Parenthood	43.8(10.6)	38.1(8.2)
FPI-dimension ILD[c]	95.6(28.9)	60.9(18.4)
Sexual Concern	25.1(10.7)	18.7(6.2)
Social Concern	33.6(8.3)	21.6(8.2)
Relationship Concern	31.5(13.9)	22.1(9.2)

[a]Higher values indicating higher level of infertility-related stress; RIP, Representations about the Importance of Parenthood; ILD, Impact on life domains

6.2 STUDY 2

6.2.1 Participants

At the first interview, 11 women (age 20–41, median 32) and 10 men (age 22–40, median 33) participated. They were diagnosed with various types of cancer: lymphoma (n=5), breast cancer (n=4), leukaemia (n=4), testicular cancer (n=3), ovarian cancer (n=3), sarcoma (n=1) and vulvar cancer (n=1). All received chemotherapy treatment, and this was most often combined with radiation therapy, surgery or anti-oestrogen treatment. The majority of the participants were in stable relationships (n=16) and half (n=11) had biological children. In addition, one man's partner was pregnant with their first child.

Two years later, nine of the women (age 23–41, median 32) and seven of the men (age 24–40, median 30) participated in a second interview. They had been treated for lymphoma (n=3), breast cancer (n=4), leukaemia (n=3), testicular cancer (n=3), ovarian cancer (n=2) and vulvar cancer (n=1). All but two had completed their cancer treatment; one woman received adjuvant anti-oestrogen therapy, and one man received chemotherapy treatment by oral administration. All who were in stable relationships at time of first interview were still with the same partner two years later. In addition, one woman who was single at the first interview was in a new stable relationship at time of the second interview. The majority had biological children (n=12), and one woman was pregnant with her first child. Most participants had gone back to their full-time work or studies, but one woman had long-term sick leave and one woman was unemployed.

6.2.2 Paper III – Main findings

The aim was to investigate newly diagnosed cancer patients' experiences of fertility-related communication and their reasoning about the risk of future infertility.

The analysis resulted in three sub-themes illustrating the process of being informed about the risk of infertility: *Getting to know*, *Reacting to the risk* and *Handling uncertainty* (Figure 5). Through the sub-themes, a main theme was embedded: *Women more vulnerable when facing risk for infertility*. This vulnerability seems to originate in that the women frequently described negative experience of the fertility-related communication, substantial concerns regarding future ability to have children and had not had the opportunity to undergo fertility preservation and therefore could not put trust in it.

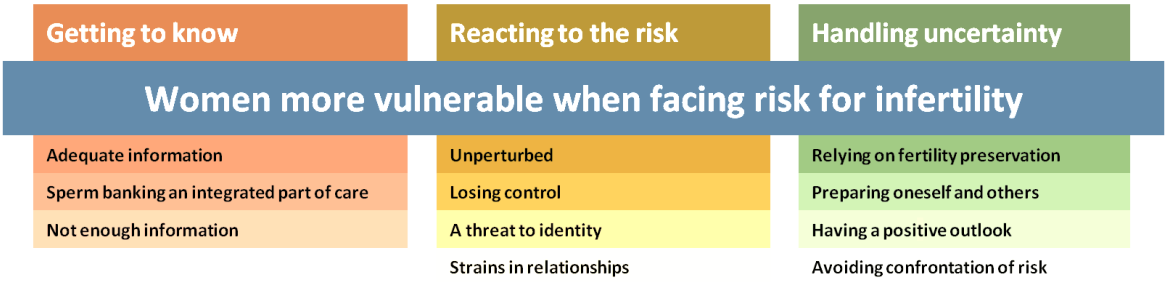

Figure 5. Illustration of main findings among men and women undergoing cancer treatment

6.2.2.1 Getting to know

In this sub-theme, the participants described how they experienced communication about the fertility-related aspects of their cancer treatment. Overall, women described negative experience of the fertility-related communication. They have had very little or no fertility-related communication with health care professionals. They tried to find explanations as to why by describing inner and outer barriers. Inner barriers included that they might have forgotten any communication about fertility or had not been receptive to it in the chaotic situation following diagnosis. They also described how they had avoided asking questions about it as they felt that the issue was sensitive to them. Outer barriers were described as having limited time with the physician, where they had to prioritize other issues instead if fertility or not knowing who among their health care professionals to ask about fertility. Others wondered if the health care professionals had assumed that they did not want children or judged them to be too old for any fertility-related discussions. The men described positive experiences of fertility-related communication. They have had the opportunity to ask questions and had communicated about fertility on several occasions: they felt that their future ability to have children had been important to their health care professionals. They

seemed to perceive sperm banking as a taken-for-granted part of the cancer treatment, alongside other routines included in their cancer treatment. The decision to bank sperm had often been taken in haste, but this was mostly seen as something positive as they therefore did not have to ruminate about it.

6.2.2.2 Reacting to the risk

This sub-theme is about how the participants reacted to being told that cancer treatment could have a negative impact on fertility. Women frequently described how the risk of infertility left them with a feeling of losing control. They were afraid of not being able to make their own decisions about whether to have a child or not after cancer treatment. They described how they felt that someone had taken away their ability to have children by not communicating with them about fertility after cancer, and therefore were denied the opportunity to participate in decisions concerning future ability to have children. Being infertile was described as a threat to identity, as life goals had to be revaluated and the thought of infertility was described as equally distressing as the cancer itself. Men also described infertility as a threat against identity, but the use of FP made it possible to lay their concerns about their future ability to have children aside. Both men and women described frictions with significant others based on differences in how the risk of infertility was perceived. But while the female participants' described how their worries about infertility had been belittled by others, male participants described how their partners were more concerned over the threat towards fertility than they were.

6.2.2.3 Handling uncertainty

This sub-theme contains descriptions of how the participants actively tried to deal with the perceived threat towards fertility. Women predominantly described handling the risk of infertility by trying to prepare themselves and others for infertility by thinking about alternative ways to achieve parenthood, such as using donated oocytes or adopting. They also tried to be positive by hoping for the best and putting trust in God. Others also took solace in that they already had children; if they had not had children, they thought that the situation would have been much worse. Only men used FP as a way to handle the perceived risk of infertility, as only men had the opportunity to use it. The men described how FP had made it possible to lay the issue of fertility after cancer aside. They felt that if they became infertile, they would be able to have children anyway. Men who had no desire to have children viewed FP as a way to keep their options open if they changed their mind later on. Both men and women described trying to avoid thinking about the risk or not wanting to talk about it with others. They also described how they did not want to ask questions about the magnitude of the risk of infertility as they were afraid of the answer.

6.2.3 Paper IV – Main findings

The aim was to explore how men and women experience life with regard to fertility and having children over the first two years following a cancer diagnosis.

The analysis resulted in the identification of four patterns of experience through time: All participants in the first group, *Continue calmly on chosen path* (1 woman and 3 men, median age 39.0), and second group, *Abandoned plans for children* (4 women, median age 32.0), had children. In the third group, *Avoiding the subject of fertility* (1 woman and 3 men, median age 28.0), one had children at time of the first interview, and at the second interview, one more had a child. In the fourth group, *Increasing struggle towards life goal* (3 women and 1 man, median age 28.5), two of the participants had children, and at the second interview one women was pregnant.

6.2.3.1 Continue calmly on chosen path

In this group the issue of fertility and having children after cancer was of little concern to the participants, and this attitude was stable throughout the two years. The participants had already had all children they wanted, and being infertile would even be convenient as they would not have to use contraceptives. However, the men had banked sperm as a way of keeping their options open if a desire to have children should arise later on. Even though the participants felt that it would be interesting to know their fertility status, none had taken any action to test their fertility as the result was of no or little importance.

6.2.3.2 Abandoned plans for children

This pattern shows a change in the plans to have children related to the cancer experience. Previous plans to have additional children had been abandoned during the two years because of the fear of cancer recurrence in connection with a pregnancy. But even though they made the decision to not have additional children themselves, they described how they would always long for another baby. The issue of fertility and having children had become sensitive and also brought up feelings of guilt over denying one's partner a biological child. The threat of infertility left the participants with a feeling of losing control; being able to choose whether to have a baby or not was regarded as essential, despite the decision to not have additional children.

6.2.3.3 Avoiding the subject of fertility

This pattern show growing concerns about the risk of infertility. When diagnosed, the focus laid first on getting well, and the issue of fertility was described as something that belonged to the future as they had no plans to have children for a while. However, over the years, their concerns about fertility had grown, and they described how they only recently had started to think about what a diagnosis of infertility would entail, such as being abandoned by partners or having to use alternative ways to achieve parenthood, such as adoption or using IVF. However, by placing the issue of fertility into the future, or by postponing fertility tests or not talking about the risk with partner, or asking questions their physician about it; they avoided

negative feelings in the present. They described how there was little to gain and much to lose if they learned that they were infertile, and they hoped that the problem would solve itself when it was time to have children. However, this standpoint had to some extent caused problems when the partner wanted to talk about the risk or tried to convince the other to take a fertility test.

6.2.3.4 Increasing struggle towards life goal

This pattern shows how fertility and having children after cancer had come to be an increasingly large part of the participants' lives. When diagnosed with cancer, infertility was described as a worst case scenario, even worse than the cancer diagnosis, and during the two years the concerns regarding ability to have biological children had grown. The participants described how they had tried to figure out their fertility status through frantic attempts to conceive or by worrisome visits to fertility clinics. There were differing opinions between partners regarding how much effort to put forth to have a child, for example, how much it was worth to pay for IVF treatment to have a sibling, or in what to do in case of recurrence during pregnancy, which caused strains in relationships. Finding common ground in communication was not always easy. Coming to terms with confirmation of being infertile was described as a struggle, as were finding alternative ways to achieve parenthood. These alternative ways included IVF treatment or adoption, and also surrogacy and uterus transplantation, even when knowing that these options were not available at present. Infertility was described as "being half" or as a sorrow over not being able to carry a child, something "as a women was supposed to do". Infertility was also viewed as a big secret only shared with the closest friends and family.

7 DISCUSSION

7.1 SUMMARY OF FINDINGS

The overall results of this thesis showed that women often had no recollection of having had any fertility-related communication with health care professionals, and women who had communicated about fertility-related aspects of their cancer care described negative experiences of the communication. While few of the women used FP, more than half of the men did so, and at the time of diagnosis, men described how this helped them to lay their concerns about future fertility aside. Women frequently described concerns about their future ability to have children and described how they tried to handle the risk of infertility by preparing themselves and thinking of alternative ways to achieve parenthood if they should become infertile. The majority of the men and women who had a pre-treatment desire for children still wanted children three to seven years after treatment. Predictors for changing from no pre-treatment desire to have children to wanting children three to seven years later was being young and childless at the time of diagnosis. Men and women described how cancer and the risk of infertility had impacted their experiences of fertility and having children. For some, the risk had been of little concern, and this had been stable over time. However, others described growing concerns about fertility and having children, which affected decisions concerning if and how to have children, caused strains in relationships and created feelings of losing control.

7.2 DISCUSSION OF MAIN FINDINGS

In the next pages, the main findings in the papers will be discussed under the following headlines: *Fertility-related communication, The risk of infertility, To handle the perceived threat of infertility, Desire for children* and *Fertility problems after cancer treatment.*

7.2.1 Fertility-related communication

One striking finding in this thesis was the sex difference regarding to what extent men and women recalled having communicated with health care professionals about fertility-related aspects of their cancer care and how they experienced it. While the majority of the men reported that they recalled having received information about risk of infertility (80%) and about FP (68%), less than half of the women could recall having had any fertility-related discussion; 48% had been informed about the risk and 14% about FP (Paper I). The cancer survivors in Paper I were diagnosed between 2003 and 2007, and as FP directed to women was less developed at that time point compared to the present time, it is possible that the identified sex difference was dependent on that fact. However, the results in Paper III, based on qualitative data gathered from patients who were diagnosed between 2009 and 2011, also

indicates a sex difference in the recall of fertility-related communication. This implies that also other reasons, other than what FP options available to women, may lie behind the difference. The sex difference in fertility-related communication has been indicated earlier in both quantitative research (Anderson et al., 2008) and qualitative research (Barbour et al., 2013; Peddie et al., 2012) likely depends on the differences in FP procedures for men and women. While sperm banking in most cases is a relatively easy and quick procedure (Stahl et al., 2012), FP for women is more complex (Rodriguez-Wallberg, 2012). FP options for women involve either a delayed treatment start of two to six weeks for cryopreservation of oocytes or embryos, or invasive procedures requiring expert knowledge, as in cryopreservation of ovarian tissue or ovarian transposition (Rodriguez-Wallberg, 2012). These limitations in FP for women can be seen as an *Environmental* factor impacting the communication between patients and professionals, as described in the patient–professional communication framework (Feldman-Stewart et al., 2005). This is supported by earlier research showing that the need for immediate initiation of treatment was a primary barrier to discussing or offering FP to women among oncologists (Forman, Anders, & Behera, 2010; Louwe et al., 2013). FP for men, however, requires no such a delay, which in turn may facilitate the initiation of fertility-related discussions. In Paper III, it was discerned that fertility-related discussions among men were closely connected with plans to undergo FP; SB seemed to be an integrated part of cancer care as appointments for SB had already been done when the subject of fertility was brought up.

Women frequently described negative experiences of fertility-related communication and had unanswered questions, while men described positive experiences, including how their future ability to have children had seemed to be important to health care professionals (Paper III). This difference has been reported earlier, showing that more women were unsatisfied with fertility discussions compared to men (50% vs. 35%) (Yeomanson et al., 2013). Research investigating oncologists' attitudes and perceptions about fertility-related communication and FP show that many oncologists feel that they have limited knowledge about FP options for women (Adams, Hill, & Watson, 2013; Louwe et al., 2013; Quinn et al., 2007). Professionals' skills, which include knowledge, are one factor described as having an impact on communication in the patient–professional communication framework (Feldman-Stewart et al., 2005). Research has shown that limited knowledge about FP for women hindered the initiation of discussions about FP options as well as the ability to have successful in-depth discussions about them (Quinn et al., 2007). This could be an explanation as to why women were not satisfied and had unanswered questions in Paper III. Another explanation why men had positive experiences of the fertility-related communication could be that the information about the risk of infertility given to men was tightly connected to a solution: sperm banking. This is in line with results showing that a positive experience of fertility-related communication was related to having been offered FP (Wilkes, Coulson, Crosland, Rubin, & Stewart, 2010). Paper III showed how not being included in decisions affecting future fertility generated feelings of losing control. Regrets of not being offered FP is a recurrent finding in

qualitative research among both men and women (Achille et al., 2006; Barbour et al., 2013; Chapple et al., 2007).

Female survivors have described how they felt that they had been denied the choice to have children by health care professionals as they had not received timely information and were not given the opportunity to undergo FP (Lee et al., 2011). The descriptions of how women did not recall receiving any fertility-related communication or were unsatisfied with it (Paper III) could be viewed from the perspective of *Goals* in the patient–professional communication framework (Feldman-Stewart et al., 2005). The framework describes how these goals are based on the patient's needs and that these are not always articulated, especially in stressful situations, such as among newly diagnosed cancer patients. It seems that the women (Paper I and Paper III) had not been able to articulate their need to receive fertility-related information. In the interviews (Paper III and Paper IV), the participants described how the issue of fertility after cancer at the time of diagnosis was secondary to the cancer and its treatment. In these situations, health care professionals play an important role in guiding the patient into identifying their needs beyond cancer, which also are described in international guidelines (Loren et al., 2013). The men's positive experience of the fertility-related communication (Paper III) is a good example of how this can be executed; the health care professionals had initiated discussions about risk of infertility and FP and presented plans for SB. As described earlier, FP is not always feasible, especially among women. However, having been involved in the decision-making regarding future fertility by counselling with a fertility specialist before treatment has been shown to reduce long-term regret about having or not having preserved fertility (Letourneau et al., 2012).

Predictors for recalling fertility-related discussions beside gender were being ≤ 35 year at diagnosis, having a desire to have children and having no children at diagnosis (Paper I). Earlier research has also identified a younger age as an important aspect in fertility-related discussions: as an predictor in the recalled receipt of information (Duffy, Allen, & Clark, 2005), as a correlate to rating fertility-related information as important (Nakayama et al., 2009; Thewes et al., 2005) and as a factor among oncologists in raising the issue with patients (Arafa & Rabah, 2011). In reproductive medicine, women's age is closely connected to the success rate of IVF (Balen, 2008), and is therefore often restricted to women under a certain age. In Sweden, public health care sets the limit at 40 years, but the limit in private health care is higher, around 42 years (Nieminen, 2015). The age limits combined with the time that is lost in connection with cancer treatment may result in a missed opportunity to make use of cryopreserved oocytes or embryo, especially among women with breast cancer, where a majority also undergo adjuvant hormonal treatment with tamoxifen, typically for five years (Harlan et al., 2006). Health care professionals may have chosen to not initiate fertility-related discussions if they judged that the woman would be too old to make use of the FP after her cancer treatment was finished, which could explain why women do not recall any fertility-related discussions (Paper I and Paper III). In the *Communication process*, the patient–professional communication framework describes the importance of silence as it gives time for reflection (Feldman-Stewart et al., 2005). However, silence may also be

explicit, when a participant does not answer a question, or implicit, when a participant avoids a topic. The lack of fertility-related communication caused irritation among the female participants (Paper III), and they wondered whether the health care professionals had judged them to be too old for fertility-related discussions or whether they had just assumed that they did not want children. It seems that the lack of fertility-related communication raised questions about why this was, and they tried to find explanations for the omission as a way to handle the situation.

7.2.2 Facing the risk of infertility

The participants in the interview study described how, at the time of diagnosis, fertility after cancer, was secondary to the cancer and its treatment (Paper III), and that they first wanted to concentrate on their immediate health and to survive the cancer. This viewpoint has been reported earlier, both among cancer survivors (Achille et al., 2006; Garvelink et al., 2013; Wilkes et al., 2010) and health care professionals (Adams et al., 2013; Peddie et al., 2012). According to the patient–professional communication framework (Feldman-Stewart et al., 2005), communication is determined by A*ttributes* such as needs as it constitute the participants' motivation to communicate. The participants described how their need for fertility-related discussions had to come behind more urgent needs, such as communicating about test results and bothersome side effects from the cancer treatment (Paper III). Nevertheless, they also described concerns about future fertility in close connection with their cancer diagnosis. These concerns were not only described as fear of losing control over the reproductive ability; they were also described as a threat towards one's masculinity or femininity. When infertility was experienced as equally distressing as cancer, participants described how these feelings had been belittled by family and friends, who said that surviving cancer was more important than having children. The same viewpoint among health care professionals can be discerned in earlier research, showing how women felt discouraged to use FP by health care professionals saying that they had much to lose and little to gain in delaying a life-saving treatment in order to do FP (Peddie et al., 2012), or by being told that they may have to "sacrifice" their fertility to cancer (Barbour et al., 2013). Holding such a viewpoint as a health care professional may induce distress among patients who feel differently. It is therefore important that health care professionals are aware that being able to have children after cancer treatment may be the most important aspect for the patient at hand.

Many of the participants described how their concerns about fertility and having children after cancer had become more pronounced over the two years (Paper IV), such as a fear of recurrence in connection with a future pregnancy or worries about being infertile and finding alternative ways to achieve parenthood. Other longitudinal studies also show increased concerns regarding fertility, such as worries about future pregnancies or that something could be wrong with the child (Carter et al., 2007), or going from not perceiving fertility as an issue to feelings of regret of not taken advantage of FP when offered (Connell et al., 2006). This change might be related to having completed cancer treatment, which allows the survivors to

form more concrete plans about the future. However, the change may also be related to different stages in life, such as age and relationship status, which have been indicated in earlier research (Crawshaw & Sloper, 2010; Wilkes et al., 2010). Also, having or not having children may be a factor in growing concerns over time (Paper IV). A study among cancer survivors showed that the intensity of the desire for children increased over time in childless patients, but decreased among patients who already had children (Geue et al., 2014).

7.2.3 To handle the perceived threat of infertility

The participants described different ways of handling the threat of infertility (Paper III), such as trying to have a positive outlook and hoping for the best, trying to prepare oneself by thinking of alternative ways to achieve parenthood in case of infertility, or by trying to avoid the issue. The avoidance behaviour described by the participants in Paper III and Paper IV was demonstrated in not wanting to ask questions about the risk of infertility or about success rate of IVF, not wanting to talk about the risk with partner and not wanting to test their fertility. The reason for not wanting to test fertility was that they feared the perceived consequences of infertility, such as being abandoned by their partner or having to rely on alternative ways to have children, such as IVF or adoption. The reluctance to test fertility has also been described earlier, and the survivors justified it by saying that they would do it when it was time to have children (Nilsson et al., 2014), that not knowing was preferable to knowing about sub-optimal fertility (Crawshaw, 2013; Eiser et al., 2011) and that a negative result could impact perceived virility (Crawshaw, 2013). Avoidance behaviour can be an effective way of handling stress when there are limited possibilities for influencing the situation (Lazarus RS, 1984). This avoidance behaviour contributes understanding of why some patients did not recall having any fertility-related communication. It is possible that health care providers had tried to initiate a discussion about fertility after cancer, but when the patient signalled that they did not want to talk about the matter, they may have chosen to leave the topic. In relation to the patient–professional communication framework (Feldman-Stewart et al., 2005) this avoidance behaviour, built upon *believes* about what would happen if diagnosed as infertile, function as a barrier towards communication.

Both men and women described how the issue of fertility and having children after cancer gave rise to relationship problems; differing opinions about if and how to have children, whether to talk about the issue or not or whether to do fertility testing caused some tensions within couples (Papers III and IV). Studies among infertile men and women who had not had cancer show that an individual's coping strategies influence the distress experienced by the partner as well as marital distress in the couple (Peterson, Pirritano, Christensen, & Schmidt, 2008). The issue of fertility may be sensitive not only for the person diagnosed with cancer, but also his or her partner. After consulting the patient, it may therefore be important to include partners in the fertility-related discussions, both at the time of diagnosis and during follow-up care.

The results of Paper III showed that descriptions of fertility-related concerns predominantly were given by women. It is possible that the explanation to this lays in women having a stronger need to nurture, as suggested by the biosocial model of fertility motivation (Foster, 2000) or that women have a stronger desire to have children, as suggested by Brase and Brase (2012). However, a recent study among female breast cancer survivors reported that women who had been able to freeze oocytes or embryos were much less preoccupied about their future fertility compared to women who had not (Corney & Swinglehurst, 2014b). Fertility preservation can be seen as a way to handle the perceived threat towards fertility. Men described how they put trust in the banked sperm (Paper III), and they described SB as a "back-up" that helped them to put concerns about future infertility aside. In qualitative studies, FP has repeatedly been described as something positive; among men it is described as a safety net (Eiser et al., 2011), an insurance for the future (Barbour et al., 2013) or as a buffer against anxiety (Crawshaw, 2013) and among women as bringing feelings of hope and a reason to live (Garvelink et al., 2013), or, in connection with radical trachelectomy, as repairing threatened femininity (Komatsu et al., 2014). Paper I showed that more than half of the men used FP (54%, n=85) and out of these men, 29 had no desire to have children at the time of diagnosis. Some of these men may have been so young that they had no concrete plans to have children at the time of diagnosis. However, the findings in Paper III provide an additional explanation. Some men with no desire to have additional children decided to bank sperm anyway, as it was a way to keep options open if they would change their mind later on; it was a way to of maintaining control over their future reproductive ability. As women use FP options to a lesser extent, it is possible that the vulnerability among women shown in Paper III depends on women not having the opportunity to use FP as a way to maintain control over future reproductive ability.

7.2.4 Desire for children

Besides the changes in concerns about fertility shown in Paper IV, Paper II showed how the desire to have children changed over the three to seven years that had passed between diagnoses and the time of study. In most cases, the participants had maintained their opinions concerning whether to have children or not, which has also been reported earlier (Canada & Schover, 2012; Geue et al., 2014). Age was one predictor for changing their mind regarding wanting or no longer wanting children three to seven year post-diagnosis, which has also been described earlier as an important factor in the desire to have children (Crawshaw & Sloper, 2010; Wilkes et al., 2010). However, the findings in Paper IV provide extended knowledge regarding the change from having a desire to have children at the time of diagnosis to not wanting children after cancer treatment. In Paper IV, women described how they had abandoned their earlier plans to have children as they were afraid of cancer recurrence in connection with pregnancy. This fear has been described earlier, together with worries about pregnancy problems and about future children's health, such as a genetic predisposition for cancer (Carter et al., 2007; Connell et al., 2006; Crawshaw & Sloper, 2010;

Nilsson et al., 2014; Pacey et al., 2013; Schover et al., 2002; Schover, Rybicki, Martin, & Bringelsen, 1999; Zebrack et al., 2004). Extensive research shows that there is no increased risk of recurrence in connection with pregnancy and no indication of increased health problems among offspring of cancer survivors (Lawrenz et al., 2012). However, there is an increased risk of pregnancy complications, such as miscarriage and pre-term delivery among female cancer survivors (Lawrenz et al., 2012). The findings in Paper IV and earlier research show how the desire to have children may be affected by fear of cancer recurrence, pregnancy problems and worries about the health of future children. In relation to the biosocial model of fertility motivation (Foster, 2000), the above described fears and worries about having children after cancer can be seen as perceived costs of childbearing. If these cost outweigh the perceived benefits of childbearing, such as achieving normality by having children (Crawshaw & Sloper, 2010; Zebrack et al., 2004), fertility motivation may go below the threshold for deciding to have a child. By being aware of these reproductive concerns, health care professionals can help cancer patients and survivors make informed decisions concerning whether to have children after cancer by providing adequate information. Women who become pregnant after cancer treatment should also be closely monitored as there is a risk for pregnancy problems (Lawrenz et al., 2012).

7.2.5 Fertility problems after cancer treatment

Paper II showed that survivors with an unfulfilled desire to have children reported lower mental health scores compared to those who had been able to have children after treatment. Earlier research among female survivors has shown that an unfulfilled desire to have children is correlated with more intrusive thoughts, more avoidance strategies and a higher level of emotional distress (Canada & Schover, 2012). Participants who had become infertile after cancer treatment (Paper IV) described a feeling of being half, or sorrow over not being able to carry a child as women were meant to do. They also described how infertility had become a secret shared only with the closest friends and family. A study among infertile couples without cancer showed that silence or secrecy about fertility problems was an attempt to protect themselves from hurtful comments or unwelcomed advice (Allison, 2011). Infertility has been described as a secret stigmatization, as only the individuals' own knowledge about their situation distinguishes them from others (Whiteford & Gonzalez, 1995). A study among male cancer survivors showed how infertility was viewed as a failure, and the men described how they tried to avoid anticipated social rejection by not being open about it (Crawshaw, 2013). The inability to talk openly about infertility has been shown to be related to high levels of reproductive concerns among female cancer survivors (Wenzel et al., 2005a). Knowing that infertility after cancer may cause concerns, sorrow and feelings of failure, health care professionals can help the cancer survivor by offering consultation if needed.

7.3 METHODOLOGICAL CONSIDERATIONS

7.3.1 Study 1

7.3.1.1 Study design and sample

The study's main strength is that it is based on a relatively large population-based sample including both male and female cancer survivors with selected diagnoses requiring treatment with a potential negative impact on fertility. By including both male and female survivors from the same population-based sample, some with the same cancer diagnoses, a unique opportunity arose that allowed comparisons between the groups. This provided new and important knowledge about sex differences, both in the recollection of fertility-related communication and in the use of FP.

7.3.1.2 External validity

External validity refers to which extent the results can be generalized beyond the investigated sample, to other populations and settings (Kazdin, 2014). The intention was to target groups of survivors who had received treatment with a possible negative impact on fertility during reproductive age. Therefore, diagnoses that are relatively common in young adult cancer patients and that usually involve treatment that has an impact on reproductive ability, such as chemotherapy treatment and/or treatment directed at the reproductive organs, were selected. The results can primarily be generalized to survivors with the cancer diagnoses selected for the study, as different treatment regimens may impact the routines regarding fertility-related communication and FP. The men and women included in the study were diagnosed between 2003 and 2007, and although FP for women was available, the options were less developed and may therefore not been considered as a viable option. Only recently has the cryopreservation of oocytes been recognized as an established method (Loren et al., 2013), and ovarian tissue cryopreservation is still considered as experimental (Rodriguez-Wallberg & Oktay, 2012b). Therefore, some caution is advised when interpreting the results as they may not be directly applicable to the present situation among female cancer patients. As the Swedish health care system enables residents to undergo tax-funded FP, caution is advised when generalizing into other health care contexts based on private health insurance.

The relatively low response rate (60%) constitutes a threat to the external validity, as it makes the sample less representative to the population (Polit & Beck, 2004). Also, fewer male cancer survivors chose to participate than women (50% vs. 67%). This sex difference in the response rate could be explained by a general difference in men and women's valuation of the studied issue—fertility after cancer. This is supported by earlier research showing that women in general had a stronger desire for children and more frequently thought about having children compared to men (Brase & Brase, 2012). It is possible that among those who could not recall having communicated about fertility, more women than men chose to participate. This in turn could be an alternative explanation to the sex difference in the recollection of fertility-related communication. Besides the sex difference in the response rate, analysis showed no difference regarding age at diagnosis, age at the time of study or

time since diagnosis between responders and non-responders. In addition, the educational level of study participants was in parity to the general Swedish population in the same age span (Statistics Sweden, 2009). As there are no other data concerning the non-responders, one can only speculate the cause of the low response rate. It is possible that those who declined to participate felt that the area of fertility was sensitive or that they had health problems, or vice versa, that those who felt that the area of fertility was of no interest to them or had no health problems declined to participate to a greater extent.

7.3.1.3 Construct and statistical conclusion validity

Construct validity refers to which degree the instrument measures the concept it claims to measure (Kazdin, 2014) and statistical conclusion to which degree conclusions about the relationship between the variables are true and reasonable (Kazdin, 2014). The survey included two validated instruments to measure mental health (SF-36) and infertility-related stress (FPI). The SF-36 is a generic instrument suitable for use among general population as well as among men and women suffering from different diseases. Nonetheless, it is possible that the scales in SF-36 were not sensitive enough to capture cancer-specific health issues and that an instrument designed to measure quality of life among men and women diagnosed with cancer had provided more specific data concerning mental health. FPI was used to measure infertility-related stress, and as it was used outside its target population, an additional response alternative was added ("Not applicable"), which may have affected the result by creating missing values in the sub-scales. However, missing values were substituted with the mean value of the score obtained in the subscale, provided that at least half the questions in the subscale were answered (Polit & Beck, 2004). In the present study, all men and women responded to the questions in FPI-dimension RIP, and participants with self-reported ongoing fertility problems also responded to the questions in FPI-dimension ILD. As no items measured the nature of ongoing fertility problems, it is possible that some participants who had just recently started trying to conceive contributed to the data. This in turn may have lowered the scores. This assumption makes the results interesting as the scores in FPI in the present study were slightly higher compared to the scores among men and women who had been referred to infertility treatment (Peterson, Newton, & Rosen, 2003). However, as the power was low (a sub-group with only 19 participants), no statistical comparison was possible.

In this study, the data about fertility-related communication and about pre-treatment desire to have children were based on the survivors' recollections which could be a threat to construct validity. Previous studies indicate that time and emotional aspects, such as the emotional strain that arises in connection with a cancer diagnosis, may affect the recollection of fertility-related discussions (Kessels, 2003). Therefore, some caution is advised when interpreting the data. Nonetheless, even if recall bias could be an explanation for the low percentage of participants having discussed the fertility-related aspects of cancer treatment, it cannot explain the differences concerning the frequency of fertility-related communication between men and women. An alternative explanation to the sex difference in the recall of fertility-

related communication could be that the majority of the men had been offered and used FP; such a concrete action may help in recalling fertility-related communication.

7.3.2 Study 2

7.3.2.1 Study design and sample

The main strength of the study is its design, in which both men and women were interviewed shortly after diagnosis and again after two years. The longitudinal design allowed for patterns of change or stability to be investigated over time (Saldaña, 2003), focusing not on a static phenomenon but instead on discovering patterns in which individuals proceed in response to a threat or a stressor and describing how these persons adjust or adapt to change (Brink PJ, 1998).

In the beginning of the study, few potential participants were identified. When investigating the matter, it was found that staff responsible for the recruitment had only approached patients that they knew had had fertility-related discussions, or who had used FP, in order to avoid giving bad news about risk for infertility. When the author of this thesis took over the recruitment, all eligible patients were approached. Participants who had not had any fertility-related communication with health care professionals were upset about it, but they also appreciated being included in the study. If they had many questions about their future ability to have children or why health care professionals not had initiated any discussions about fertility, they were encouraged to talk with their physician about the matter. At the start of the study, 21 men and women were included, but two years later, five of the participants had died, moved abroad or declined further participation. It is possible that if more patients had been included in the initial recruitment, other patterns of experiences may have been identified, especially if more men and women who were single had been included. In some of the interviews, partners to the participants were present, and it is possible that this may have influenced the participants' narratives. However, the participants who had partners present also described friction in the relationship related to the risk of infertility and about having children in the future.

In order to determine the study's trustworthiness, the criteria's described by Graneheim and Lundman have been followed (Graneheim & Lundman, 2004). They propose three criteria for judging the rigor of qualitative research: *Credibility*, *Transferability* and *Dependability*.

7.3.2.2 Credibility

Credibility refers to how well data and processes of analysis address the intended focus (Graneheim & Lundman, 2004). The prolonged engagement obtained through the longitudinal design helped in building trust between the researcher and participants, and this was also manifested in how the second interview was generally longer and richer. The first interview was conducted in the cancer ward in connection with treatment, and one could

argue that this did not create a setting that was homely or that invited confidence. However, privacy was guarded by conducting the interviews in a secluded room with a "do not disturb" sign on the door. The interviewer was also not a part of the participants' health care team, nor dressed as one. The variation of participants concerning age, sex, desire for children, parenthood status, relationship status, education and diagnosis enabled allowed for the experiences of fertility-related communication and fertility after cancer to be captured from different angles.

However, one shortcoming was that only two interviews were conducted, the first a short time after cancer diagnosis and the second two years later. It is possible that other patterns of experience would have been identified if the participants had been interviewed repeatedly at shorter intervals, or if they were followed over a longer period of time. Lincoln and Guba (Lincoln & Guba, 1985) highlight the importance of analysing deviant or negative cases. In the present study, men and women who had no desire to have children were also included. By doing so, we were able to capture their experience of fertility-related communication and fertility, and in this, we could see that even if they had no desire to have children, they wanted to receive information about fertility. Also, women described how retained fertility was not only seen as the ability to have children, but also as a way of maintaining control. In addition, we could see that two participants who initially had no desire to have children changed their mind during the two years.

Interviewers and interpreters of data are co-creators of results (Graneheim & Lundman, 2004; Jootun, McGhee, & Marland, 2009), and with this in mind, those working on the study repeatedly had meetings to discuss data collection, data analysis and the presentation of the data. Both the raw data (the transcribed interviews) and the processed data (identified meaning units, codes, categories and themes) were discussed. As the authors had different backgrounds, such as clinical backgrounds in cancer care and reproductive medicine and in cancer research, taken for granted aspects were challenged and brought into light. By this the authors become aware of their posture towards data and analysis (Lincoln & Guba, 1985).

In the analysis of the longitudinal data, a strategy was formed specifically to address the study aim, which was to explore experiences over time. By systematically analysing data in three phases, change or stability through time could be studied at both the individual level and the group level. It is possible that the first understanding of the data obtained in Phase 1 affected the structured analysis in Phase 2. Continually throughout the analysis, alternative interpretations of the findings were discussed, especially the patterns leading to the two last groups: *Avoiding the subject of fertility* and *Increasing struggle towards life goal*. It is possible that the two groups mirror the same trajectory over time but at different stages, depending on how ready they were to concretize their plans to have children. If the same participants had been followed for a longer time period the participants in *Avoiding the subject of fertility* may have shown the same pattern as those in *Increasing struggle towards life goal* when they started to build a family.

7.3.2.3 Dependability

Dependability refers to the stability of data over time and conditions (Graneheim & Lundman, 2004). As the data collection spanned a time period of four years, it was important that the data gathering was consistent. In order to minimize inconsistency, an interview guide was followed. However, the interviewer's own interviewing skills were developed over the period, and at the end of the data collection period, the interviewer allowed more silence and recuperation in the interviews, which may also be an explanation of the richer data. As mentioned above, the first interviews were all conducted at cancer wards. The conditions surrounding the second interviews differed among the participants. Most of the interviews were conducted in the participants' homes, while others were at the hospital in connection with a follow-up or, for example, at the participants' workplace. These differences in conditions may have impacted the interviews; interviews in anonymous rooms at the hospital do not create an environment that encourages confiding as much an interview in the participant's own kitchen. However, as the participants chose the interview location, an interview in one participant's home may have not been as relaxed as it was for someone else.

7.3.2.4 Transferability

Transferability refers to the extent to which the findings that can be transferred to other contexts or settings (Graneheim & Lundman, 2004). The results may be transferable to other men and women of reproductive age who receive a curative cancer treatment with a negative impact on fertility. The results from Paper III may also be transferable to other groups who receive a treatment that may have a negative impact on fertility, such as patients with multiple sclerosis undergoing stem cell transplantation or patients with rheumatic diseases requiring high doses of NSAIDs or cyclophosphamide. However, as the results from Paper IV are closely connected with the cancer experience, we advise caution in transferring the results to other contexts.

8 CONCLUSION

This thesis shows that the majority of both male and female cancer survivors who had a pre-treatment desire to have children still wanted children after completing cancer treatment. However, there were marked sex differences regarding fertility-related communication and in the use of FP, all to the detriment of women. These deficiencies seemed to make the women particularly vulnerable; they did not use FP and could therefore not put their trust in it helping them to have biological children after completing treatment. As the women also did not receive adequate information, they had unanswered questions about fertility after cancer and expressed disappointment over not being included in the discussions. Over the two-year time span both men and women's described growing concerns about fertility and having children after cancer. The risk of infertility had affected decisions about whether to have a child and in what way, and they described how this gave rise to relationship problems and feelings of losing control. Not being able to have children affected perceived masculinity or femininity and gave feelings of sorrow, and an unfulfilled desire to have children was correlated with worse mental health.

9 CLINICAL IMPLICATIONS

Even if the preconditions for female FP can be an explanation to the lack of satisfying communication between health care professionals and female cancer patients, women have to know about the risk of infertility in order to make informed decisions about future fertility. The deficiencies in fertility-related communication seem to create a ground for vulnerability among women; uncertainty about future fertility paired with disappointments over not being included in discussions lead to a feeling of losing control. In cancer care, it is vital to remember that in the stressful situation following a cancer diagnosis, patients are in a state of dependability. They have to trust health care professionals to identify needs that they themselves are not able to identify or articulate. Being young and having no children are associated with changing desires regarding wanting children years later. By being aware of this, health care professionals may help patients in this group to understand the need to consider FP, even if they do not perceive future fertility as important at the time of diagnosis and during the planning of initial cancer treatment.

Worries about the risk of cancer recurrence in connection with a pregnancy caused women abandon their plans to have children. This has also been reported earlier, together with fear of pregnancy complications and health problems for future children. By providing adequate information regarding risks in connection with having children after cancer help survivors to make informed decisions about future childbearing. As the experience of fertility and having children after cancer may change over time, the subject should be introduced not only at the time of diagnosis but also after cancer treatment during follow-up care. The results showed that different perspectives between patients and partners regarding the risk of infertility and having children after cancer sometimes gave rise to relationship problems. By including partners in discussions concerning the risk of infertility, couples in need of extra support could be identified. However, as the area of fertility after cancer may be sensitive, it is important to first consult with the patient before offering joint consultation.

In clinical practice, clear guidelines and close collaboration between cancer clinics and reproduction clinics may help safeguard patients' future ability to have biological children. In view of the complexity of FP for female patients, health care professionals in both in cancer and reproductive care should set aside extra time to discuss fertility issues with women of reproductive age diagnosed with cancer. The use of decision aids may also be of help in the discussions regarding FP.

10 FUTURE RESEARCH

Based on the findings in in Study 1, it would be interesting to follow up cancer survivors' perceptions of the communication by investigating oncologists and haematologists' experience of fertility-related communication. Earlier research has investigated physicians' practice behaviours, attitudes and barriers to some extent, but no studies conducted in the Nordic countries have been found. Also, these studies have not specifically investigated practice behaviours regarding the patient-based sex differences in fertility-related communication that were found in Studies 1 and 2. Studies including registered nurses are also called for. Cancer care is a multi-disciplinary area where the registered nurse plays an important role in the psychosocial care of cancer patients. Few studies have investigated registered nurses' experiences of fertility-related communication. Extended knowledge about their role in fertility-related communication may lay the ground for increased collaboration between the disciplines, aiming to improve fertility-related communication, and in the end, optimize cancer survivors' possibilities of having biological children after cancer treatment.

The results showed how men and women's described growing concerns over time. Study 2 only followed the participants over two years, and there is limited knowledge about cancer survivors' experience of trying to conceive or going through pregnancy and childbirth after cancer. Studies investigating survivors' experiences of the contact with health care professionals at cancer clinics, reproduction clinics and maternity clinics may provide new knowledge about informational needs and the need for support. This is especially important as the number of men and women diagnosed with cancer before they start or complete their families is increasing. The use of fertility preservation option is also becoming more common, which in turn will increase the number of men and women returning to reproductive clinics for infertility treatment with cryopreserved sperm, oocytes or embryo.

The findings in this thesis showed that the risk of infertility and having children after cancer not only affected the men and women who received a cancer diagnosis but also their partners. In Study 2, the participants reported strains in relationships due to differing opinions about the risk of infertility, future pregnancies or fertility testing. It is recommended that future research also include partners as the dynamics in relationships impact patients/survivors' experiences of the matter.

11 SUMMARY IN SWEDISH/SVENSK SAMMANFATTNING

Bakgrund I norden lever idag drygt 78 000 personer som behandlats för cancer i åldern 44 år eller yngre. Tidigare forskning visar att cancererfarenheten i de flesta fall inte påverkar viljan att i framtiden bilda familj, och många beskriver att deras önskan att få barn växt sig starkare genom erfarenheten. Tyvärr finns risk för infertilitet efter genomgången cancerbehandling och studier visar att födelsetalen bland dem som behandlats för cancer är mellan 24% till 54% lägre jämfört med kontrollgrupper. Cytostatika har en toxisk inverkan på äggstockar och spermaproduktionen. Också andra problem kan uppstå i samband med cancerbehandling, såsom nedsatt blodcirkulation i livmoder efter strålbehandling och medföljande risk för missfall hos kvinnan, eller nervskador efter kirurgiska ingrepp i bäckenområdet och medföljande erektionsproblem hos mannen. För att öka chanserna att få biologiska barn i framtiden finns fertilitetsbevarande åtgärder tillgängliga. För män är infrysning av sperma en relativt enkel och välbeprövad åtgärd men fertilitetsbevarande åtgärder för kvinnor är mer komplexa. Infrysning av ägg eller embryos tar 2-6 veckor och är då inte alltid möjlig att genomföra. I dessa fall kan man överväga infrysning av äggstocksvävnad, men metoden är ännu experimentell. Forskning visar att både män och kvinnor är positiva till att diskutera fertilitetsrelaterade aspekter av cancerbehandlingen i samband med diagnos, och bland män har forskning visat att infrysning av sperma ger en känsla av trygghet för framtiden. Trots detta visar flera rapporter att det finns brister i den fertilitetsrelaterade kommunikationen, och både män och kvinnor uttrycker besvikelse över att de inte har erbjudits fertilitetsbevarande åtgärder.

Syfte Avhandlingens övergripande syfte var att undersöka uppfattningar och upplevelser av fertilitetrelaterad kommunikation bland män och kvinnor som diagnostiseras med cancer i reproduktiv ålder i Sverige. Ett ytterligare syfte var att undersöka upplevelser av att få cancerbehandling med en möjlig negativ inverkan på fertilitet och hur detta upplevs över tid.

Metod Avhandlingen baserades på två studier: en kvantitativ enkätstudie bland personer som behandlats för cancer tre till sju år tidigare och en kvalitativ longitudinell intervjustudie bland nydiagnostiserade cancerpatienter. I Studie 1 besvarade 484 personer (328 kvinnor och 156 män, 60% svarsfrekvens) som behandlats för cancer tre till sju år tidigare en studiespecifik enkät som även inkluderade standardiserade instrument för att mäta mental hälsa (SF-36) och infertilitetsrelaterad stress (FPI). I Studie 2 deltog nydiagnostiserade cancerpatienter i semistrukturerade intervjuer vid två tidpunkter, kort tid efter cancerdiagnos (11 kvinnor och 10 män) och två år senare (9 kvinnor och 7 män). Intervjuerna rörde sig kring följande områden; erfarenheter av fertilitetsrelaterad information och fertilitetsbevarade åtgärder, upplevelsen av att får en cancerbehandling som kunde påverka fertiliteten och tankar kring att skaffa barn i framtiden.

Resultat Studie 1 visade markanta könsskillnader i fertilitetsrelaterad kommunikation; medan majoriteten av männen kunde påminna sig om att ha diskuterat risken för infertilitet (80%)

och fertilitetbevarande åtgärder (68%), gjorde färre kvinnor det (48% respektive 14%). Dessutom hade mer än hälften av männen frusit in sperma (54%), medan endast 2% av kvinnorna hade använt sig av någon fertilitetsbevarande åtgärd. Majoriteten av de som hade barnönskan vid tiden av diagnos ville fortfarande ha barn tre till sju år senare. Dessutom hade 17% av dem som inte hade någon barnönskan vid tiden för diagnosen ändrat sig till att vilja ha barn. Studie 2 visade att kvinnor generellt har en negativ upplevelse av den fertilitetsrelaterade kommunikation medan männen upplevde att de hade fått omfattande information och hade uppmuntrats till att frysa in sperma. Både män och kvinnor beskrev hur risken för infertilitet hade påverkat deras upplevelser under de två åren, från att vara av föga intresse till att påverka beslut angående framtida barnafödande, orsaka relationsproblem och skapa känslor av att förlora kontrollen.

Slutsats Risken för infertilitet efter cancer kan ge upphov till reproduktiv oro bland både män och kvinnor och resultaten visar att kvinnor är särskilt sårbara då de i lägre utsträckning erhåller fertilitetsrelaterad information och använder sig av fertilitetsbevarande åtgärder. Med tanke på komplexiteten i de fertilitetsbevarande åtgärderna riktade till kvinnor behövs tydliga riktlinjer och nära samarbete mellan cancerkliniker och reproduktionskliniker för att förbättra den fertilitetsrelaterade kommunikation med kvinnor i fertil ålder.

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